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USES AND LIMITATIONS OF ESTROGENS IN GYNECIC PRACTICE

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Estrogens constitute a diverse group of chemical compounds capable of producing estrous phenomena in experimental animals and reproduction in woman, to a great degree the physiologic functions which are attributed to the follicular hormone of her ovaries.

There are two general classes of estrogens: (1) those which are identical chemically with the steroids extracted from the ovaries, placentas or body fluids, i. e., hormones, and (2) those synthetic pharmacologically active agents which bear no structural chemical likeness to natural hormones.

All three of the estrogenic hormones—estrone, estriol and estradiol—have been extracted from woman's urine and are available commercially as free steroids or as esters. During the past three years estrogenic compounds derived from stilbene, particularly diethylstilbestrol and its esters, have been subjected to broad clinical investigations looking toward their release into commerce by the Food and Drug Administration.

The primary pharmacologic action of estrogens is on the genital system: endometrial, cervical and vaginal epitheliums; myometrium; endometrial and myometrial vascular systems, and the parenchyma of the breasts. Secondary effects are produced in the skin and its appendages, the peripheral vascular bed and, perhaps, the osseous system. Reciprocities in function exist between estrogens, the anterior lobe of the pituitary gland, the adrenals and thyroid. No evidence has been submitted that estrogens stimulate ovarian function. There is good reason to believe, however, that they may depress this function by means of effects on the pituitary. These last two considerations qualify their therapeutic role as being a substitutional or complemental one rather than one which permits stimulation of hypofunctioning ovaries.

In general, the gynecic conditions in which estrogens have been employed on presumed rational indications are (1) substitutional or complemental therapy in those instances of adolescent or adult ovarian failure wherein the functional pathologic condition is intrinsic to the ovaries themselves; (2) in the treatment of local hypoplasias of the accessory sexual system; (3) as antagonistic therapy in hyperfunctional states of other glands, such as the pituitary or adrenals, and (4) for specific local effects on certain tissues, i. e., the vaginal epithelium, the estrogens being employed as pharmacologic agents rather than as means of treating endocrine disease.

In these various therapeutic applications estrogens have been administered effectively by various routes: by mouth, intramuscularly, topically applied to the vaginal and the nasal mucosa, by dermal inunction and by the subfascial implantation of sterile pellets of compressed crystals of hormone. None of these methods permit, doubtlessly, an entirely efficient or economical duplication of normal physiologic levels of estrogenic function.

My purpose in this communication is a consideration of uses and limitations of estrogenic therapy in gynecology when based on the aforementioned and apparently rational indications.

ESTROGENIC THERAPY IN OVARIAN FAILURE

Diverse grades of ovarian failure result from numerous causes, some of which are intrinsic to the ovaries while others are related to primary aberrations in other glands or are due to strictly extra-endocrine causes. An ideal therapy would permit the salvage of both the germinal and the endocrine functions of ovaries, i. e. would induce or reinstitute normal fertile ovarian cycles. When there is resort to substitutional or complemental therapy with estrogens, the immediate result may be quite satisfactory from an endocrine point of view, but this therapy cannot substitute for the germinal failure of ovaries. Estrogenic therapy is rational only in hypoovarianism due to intrinsic ovarian failure, such as that which results from surgical or roentgenologic damage, pelvic disease or tumors or sexual aging. Hypoovarianism due to thyroid, adrenal or pituitary disease or resulting from constitutional impairment should be handled, if possible, by therapeutic attention to the primary cause rather than by substitutional therapy at the ovarian level. If apparent or real ovarian failure is related to inadequate endometrial function, complemental therapy with ovarian steroids may constitute a rational therapeutic approach.

When there exist severe grades of intrinsic ovarian failure, of either estrogenic or corpus luteum type, substitutional therapy with estrogens or with estrogens and progesterone, regardless of how dramatic the immediate endocrine responses are, has obvious limitations: 1. Complete substitution year after year for the endocrine functions of the ovaries, similar in kind to that necessary with thyroid substance for hypothyroidism or with insulin for diabetes mellitus, imposes a financial burden which few patients can assume. 2. If and when treatment is stopped, regressional alterations promptly follow which destroy for the most part the accomplishments of therapy; the combined use of estrogens and progesterone under these circumstances is said to lessen the regressions which follow withdrawal of therapy. 3. Despite most intensive therapy of this sort, patients remain sterile.

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These aforementioned limitations delineate no clear-cut gynecic applications of prolonged substitutional therapy. Fortunately, ovarian deficiency rarely impairs health or somatic efficiency. The cosmetic inelegance of the young woman with well defined adolescent hypo-ovarianism constitutes one of the few conditions, if not the only one, in which some attempt at limited employment of complete substitutional therapy seems indicated at present. The rationale of therapy in this condition is (1) to curb abnormal somatic overgrowth, common in these patients, by effecting epiphysial closures, a therapeutic hope not established as yet as a fact; (2) to bring about some degree of sexual attractiveness of the patient, which accomplishment affords salutory psychic alterations, and (3) to produce genital growth and development in the hope that the ovaries may become capable of yielding full, normal responses to intrinsic pituitary influences or to those afforded by an adequate gonadotropic therapy.

The use of full substitutional doses of steroids for the sole purpose of regulating the cyclicity of uterine flowing is condemned as being meddlesome and unnecessary. Only when too prolonged or too frequent episodes of uterine bleeding produce a drain on the hemopoietic system is one justified in the employment of an empiric hemorrhagenic-hemostatic schedule of endocrine therapy. The effectiveness of a system of cyclic steroid therapy, embracing the use of estrogens and progesterone, in controlling menometrorrhagia of young women has been established. Any therapy which will permit symptomatic handling of excessive uterine bleeding of young women without impairing their fertility in the future is a valuable one. This fact, however, does not weaken the general statement that, at present, there is too much endocrine therapy of the menstrual cycle and too few attempts at rational endocrine assessments of patients.

In the physiologic hypo-ovarianism of the climacteric, therapy with estrogens is valuable at times in facilitating the hormonal adjustments of a minority of patients. The employment of dosages comparable to those used in complete substitutional therapy is unnecessary and actually harmful if therapy is prolonged. The continued use of these large doses of estrogens can and will delay, and otherwise complicate, the physiologic process of sexual aging. Our progress in geriatrics has not been such that attempts to delay old age are advisable. Troublesome menstrual irregularities and generalized edema due to disturbances in the metabolism of water and electrolytes may follow injudicious estrogenic therapy at this time. Overstimulation of the aging endometrium may enhance the incidence of carcinoma.

All therapy at the climacteric should be in line with the general therapeutic desideratum: to lessen, but not completely substitute for, the physiologic ovarian deficit of those women in whom the secondary hormonal adjustments are proceeding too slowly, i. e. palliative but not full replacement therapy. Estrogenic therapy should be limited in its duration to several months; dosages should be kept small and should be administered orally if possible; if patients have bleeding cycles, therapy should be calibrated with these cycles, estrogens being withdrawn during expected episodes of bleeding lest menstrual irregularities ensue.

Relatively low grades of estrogenic deficiency or moderate degrees of lowered endometrial receptivity may result in incomplete "priming" or vascularization of the endometrium, with the result that minimal or no progestational alterations occur. Such apparent intercurrent ovarian failure may be transformed eventually, owing to possible endometrial functions in steroid metabolism, into more real disturbances of ovarian function, i. e. corpus luteum failure. Some evidence has been presented that cyclic steroid therapy with estrogens and progesterone, or perhaps with estrogens alone, permits therapeutic salvage of patients with functional irregularities of uterine bleeding and endocrine sterility related to these etiologic factors. In these instances, therapy may be regarded as being complemental: ovarian function is complemental until such time that spontaneous adjustment can be made.

ESTROGENIC THERAPY OF LOCAL HYPOPLASIAS

Generalized hypoplasia of the sexual system is characteristic of severe estrogenic failure originating during adolescence and, likewise, distinct regressional alterations in the genital apparatus are associated with intercurrent estrogenic failure during the adult period. When, however, sexual hypoplasia is limited to a particular organ or organs, as the uterus or breasts, in women otherwise well feminized, it is found usually that the end organs and not the ovaries are at fault. Intensive estrogenic therapy designed to develop these hypoplastic organs is usually unsuccessful and may result in damage to intrinsic ovarian function. In a number of women who exhibited no evidence of ovarian deficiency except rudimentary uteri we have been unable to demonstrate any uterine enlargement from injections of estradiol benzoate or dipropionate in daily doses as large as 15,000 rat units for as long as three months. Similar experiences have occurred in the treatment of unilateral hypomastia with estrogenic ointments.

When, however, a patient with typical adolescent hypo-ovarianism is concerned chiefly by the cosmetic limitations imposed by the associated hypomastia, gratifying temporary results, and some permanent benefit due chiefly to massage, may be obtained from the local use of estrogenic ointments. This method of administration of estrogens permits concentrations of the dosage at the site of desired action. All the effects obtained from the inunction of estrogenic ointments are not local, however, as 1 of our cases illustrates:

> A woman aged 24 years had the typical body build of well defined adolescent hypo-ovarianism and her uterus was of almost rudimentary proportions. She had never experienced uterine bleeding. The nightly inunction of a drachm (4 Gm.) of ointment containing 3,000 rat units of estradiol benzoate into the skin about each juvenile breast not only resulted in mammary hyperplasia but also, after three months of therapy, sufficient uterine hyperplasia had occurred to permit the patient's first episode of uterine bleeding.

ESTROGENIC THERAPY DESIGNED TO DEPRESS HYPERACTIVITY OF OTHER GLANDS

Theoretically, intensive estrogenic therapy should be of value in depressing hyperfunctional states of the anterior pituitary and in overriding virilizing effects produced by hyperactivity of the androgenic elements of the adrenal. While it is believed generally that large doses of estrogens are capable of depressing the moderate hyperactivity of the endocrinotropic influences of the pituitary which characterize climacteric failure of the ovaries, clinical experience has not found this therapy to be of any value in combating hyperpituitary giantism or the symptoms and signs of pituitary basophilism. Likewise, estrogens have not been demonstrated to be effective in the treatment of hirsutism in general or as endocrine antagonists in virilizing syndromes arising from adrenal disease.

ESTROGENIC THERAPY FOR LOCAL VAGINAL EFFECTS

Special epithelial effects of estrogens have been adapted to an effective therapy of gonorrheal vaginitis of childhood and to nonspecific postmenopausal vaginitis. In neither of these conditions is the indication for therapy a truly endocrine one, since the hypo-ovarianism and the atrophic state of the vaginal epithelium is normal at these physiologic epochs. Estrogens are used here similarly to any other pharmacologically active agents: their specific action is concerned with vaginal cornification and the production of vaginal acidity, both of which effects an increase in the resistance of the host to the infecting organisms. Dosages of estrogens employed in this therapy can and should be kept low enough to avoid general endocrine effects, such as premature adolescent phenomena in the child or the return of uterine bleeding in the climacteric woman. The fact that treatment is necessary for only six to eight weeks, as a rule, makes it practical and usually free from undesired side effects.

Some gynecologists have employed these vaginal effects of estrogens, usually locally applied, in the preoperative preparation of postmenopausal women for vaginal procedures. It has been stated that the cornification, vaginal acidity and increased vascularity which result from this therapy have facilitated postoperative healing of the vaginal tissues.

EMPIRIC AND CONTRAPHYSIOLOGIC USES OF ESTROGENS

A large amount of estrogenic therapy at present is founded only on the empiric association of certain symptoms with the presumed existence of significant ovarian failure. This type of therapeusis, if it employs potent agents in effective doses, is likely to oppose the intrinsic function of ovaries and to upset their hormonal reciprocities with other glands. Two practices in recent organotherapeusis which are employed somewhat widely illustrate what is meant by contraphysiologic usage.

Some workers report good results from intensive estrogenic therapy in instances of "menstrual migraine." Their plan of treatment is to circumvent these headaches by postponing or suppressing menstruation. To this end doses of from 10,000 to 15,000 rat units of estrogen are given daily for from three to four weeks or longer. Menstrual irregularities occur commonly through disturbances produced in the gonadopituitary reciprocities, which are temporary, however, unless therapy is continued for long periods of time.

Many of the recent studies of so-called "idiopathic" or "essential" dysmenorrhea accept the occurrence in this condition of fundamentally normal ovarian function. Some workers have advised the use of repeated injections of estrogens as large as 10,000 rat units every third day for from three to ten doses, beginning these at the end of flowing, to override or inhibit corpus luteum function; relief of dysmenorrhea has been correlated by them with such a contraphysiologic effect. They described the dysmenorrhea as returning, however, quite promptly with the cessation of therapy. This type of treatment seems neither practical nor rational.

SUMMARY AND CONCLUSIONS

Estrogens have a definite, though restricted, role in gynecic therapy. Full substitutional therapy for severe or complete ovarian failure permits striking endocrine responses but has little practical value, since germinal failure (sterility) is not altered. When therapeutic schedules for estrogenic substitution or complementation are limited in scope and in proposed duration (adolescent ovarian failure and intercurrent episodes of relative ovarian failure producing some irregularities of bleeding and/or endocrine sterility), presently available estrogenic hormones, despite expense, permit practical applications. These hormones, likewise, permit worth while and not too expensive applications in the undesired symptomatology of certain climacteric women and in childhood and senile vaginitis.

Nonhormonal estrogens (of the diethylstilbestrol group), if released by the Food and Drug Administration, would circumvent only one of the therapeutic limitations of estrogens: their relative expense. Being orally active, cheap and highly potent, uncritical use of them by physicians and self medication with them by patients would add, doubtlessly, to an already widespread contraphysiologic and empiric estrogenic therapy.

ANDROGEN THERAPY IN GYNECOLOGY

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Synthetic testis hormone (testosterone propionate) is being used with increasing frequency in the treatment of a number of functional gynecologic conditions. We have previously reported on its use in the treatment of the menopausal syndrome,[1] functional menometrorrhagia,[2] dysmenorrhea,[3] premenstrual tension,[4] pain of ovulation and endometriosis, and functional mastopathies.[5] Our experience with androgens in gynecologic therapy, which extends over a period of more than four years and is based on a series of 422 cases, has convinced us that their use as therapeutic agents has a sound rationale and a well defined place in our endocrine armamentarium. However, like so many other valuable therapeutic agents, their use is not unattended by harmful potentialities unless specific indications are observed and appropriate safeguards employed. Fortunately, the range of biologic effects exerted by these hormones, the threshold of tolerance and the objective criteria for regulating the dosage have been clearly enough defined to warrant recommending their use in the treatment of selected types of gynecologic endocrine disorders.

Here we wish to present our observations of (*a*) the endocrinologic effects of administration of androgen to women; (*b*) the therapeutic properties of androgens; (*c*) the signs and symptoms of overdosage, and (*d*) the methods that can be used which make it possible to utilize the therapeutic properties of these hormones without inducing the undesirable virilization (arrhenomimetic) effects.

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The following pharmaceutic houses supplied the androgens used in this study: Schering Corporation, Bloomfield, N. J., testosterone propionate (Oreton), methyl testosterone (Oreton-M), pregneninolone (Pranone) and Ciba Pharmaceutical Products, Inc., Summit, N. J., testosterone propionate (Perandren) and methyl testosterone (Metandren).

1. Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. **37**: 488, 1937.
2. Geist, Salmon and Gaines.[14] Salmon, Geist, Gaines and Walter.[15]
3. Salmon, U. J.; Geist, S. H., and Walter, R. I.: Am. J. Obst. & Gynec. **38**: 264, 1939.
4. Geist, S. H.: J. Clin. Endocrinol. **1**: 154, 1941. Salmon, Geist and Walter.[8] Salmon.[7]
5. Salmon, Geist and Walter.[8] Salmon.[7]

MATERIAL AND METHODS

This report is based on the observation of 422 patients who were treated with various androgens, namely testosterone, testosterone propionate, ethinyl testosterone and methyl testosterone. These cases included normally menstruating women and those presenting a variety of gynecologic disorders, namely functional uterine bleeding, uterine fibromyomas associated with menorrhagia, dysmenorrhea, premenstrual tension, mastalgia, endometriosis and the menopausal syndrome.

METHODS OF ADMINISTRATION

The methods of administration in this series have been (*a*) intramuscular (testosterone propionate), (*b*) enteral (testosterone and methyl testosterone), (*c*) sublingual absorption (testosterone in propylene glycol) and (*d*) subcutaneous implantation (crystals and pellets of testosterone and testosterone propionate).

Although preliminary investigations were performed with a number of androgens, only three (testosterone, testosterone propionate and methyl testosterone) were found to be sufficiently potent to be effective. Of these, testosterone propionate was found to be the most potent when administered intramuscularly or subcutaneously. The majority of our studies were performed with this compound.

ENDOCRINOLOGIC EFFECTS OF TESTOSTERONE PROPIONATE IN WOMEN

In our attempt to determine the biologic properties of testosterone propionate, the doses were varied widely. Patients were given individual doses varying from 5 to 100 mg. for periods varying from two weeks to eight months. Total doses ranged from 60 to 3,200 mg. Of the 422 patients in this series, 245 received 300 mg. or less, 85 received doses ranging from 300 to 600 mg. and 92 received from 600 to 3,200 mg. It soon became apparent that the biologic effects induced by testosterone propionate varied, depending on the dosage administered and on the time of the menstrual cycle during which the hormone was given.

Effect of 500 Mg. or More of Testosterone Propionate per Cycle.—Doses of 500 mg. or more per cycle cause (*a*) inhibition of the gonadotropic hormone activity of the hypophysis;[1] (*b*) suppression of follicular growth, ovulation and corpus luteum formation;[6] (*c*) inhibition of the formation of estrogen and progesterone and excretion of pregnandiol;[7] (*d*) suppression of menstruation;[8] (*e*) abolition of the normal cyclic endometrial patterns leading to endometrial hypoplasia or atrophy;[9] (*f*) involutional changes in the vaginal mucous membrane characteristic of deprivation of estrogens,[10] and (*g*) virilization phenomena, namely hair growth on the face, extremities and occasionally on the lower part of the abdomen, deepening of the voice and, in some cases, enlargement of the clitoris.

Effect of 300 Mg. or Less per Cycle.—When testosterone propionate is administered in doses of 300 mg. or less during one cycle (approximately twenty-eight days), the inhibitory effects do not usually occur. Menstruation is not suppressed and the endometrium usually reveals no regressive changes in the microscopic pattern, indicating that the follicular phenomena in the ovary (ovulation and estrogen and progesterone formation) have not been inhibited. The 500 mg. dose per cycle appears to be the approximate threshold for suppressive effects, providing the total dose is distributed during the entire cycle or given during the first ten days of the cycle before the hypophysis has secreted gonadotropin for the current cycle or before the gonadotropin has been able to exert its action on the ovary. Similar amounts of hormone administered during the latter half of the cycle do not suppress the following menstrual period. Experimental studies indicate that the suppressive action of the hormone is achieved by inhibition of the gonadotropic activity of the hypophysis with consequent suppression of ovulation and production of estrogen and progesterone by the ovary.[11] It becomes understandable, therefore, why an amount of hormone which is suppressive (500 mg.) during the first two weeks of the cycle (before ovulation has occurred) has no such inhibitory effect on the current menstrual phenomena if administered during the last two weeks of the cycle. It has been found, furthermore, that one can produce the same suppression of menstruation by concentrating a massive dose (approximately 1,000 mg.) during the first five or six days of the cycle.

RELATION OF DOSAGE TO ARRHENOMIMETIC PHENOMENA

Experimentation with various doses of testosterone propionate revealed the fact that, if menstruation is suppressed by the hormone, patients are likely to notice some hypertrichosis, deepening of the voice and some enlargement of the clitoris. These phenomena have been observed by a number of investigators.[12] Our studies have shown that there is a fairly well defined dosage threshold for these phenomena which, for the average woman, is approximately 500 mg. of testosterone propionate a month. When this monthly dose is exceeded, the incidence of arrhenomimetic phenomena is approximately 21 per cent. Below this dosage level, the incidence of arrhenomimetic effects drops rapidly. When administered in doses of from 250 to 300 mg. a month, the incidence is approximately 1 per cent. Smaller doses (from 50 to 250 mg. a month), in a series of 179 cases, produced none of these arrhenomimetic effects.

THERAPEUTIC PROPERTIES OF TESTOSTERONE PROPIONATE

A review of the endocrinologic effects resulting from the administration of androgens to cyclic women makes it become clear that there is available in testosterone propionate a substance which has powerful suppressive effects on the entire female endocrine system and, by virtue of this, great therapeutic potentialities. A fact of great significance, which adds to its value as a therapeutic agent, is the range of gradations of biologic effects which appear to be dependent on quantitations of dosage. Thus it has been established that the threshold for suppression of the gonadotropic activity of the hypophysis, with its consequent inhibitory action on

6. Geist, S. H.; Gaines, J. A., and Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. **44**: 319, 1940.
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11. Geist, S. H.; Salmon, U. J.; Gaines, J. A.: and Walter, R. I.: Biologic Effects of Androgen (Testosterone Propionate) in Women, J. A. M. A. **114**: 1539 (April 20) 1940. Salmon (footnotes 1 and 7).
12. Foss, G. L.: Lancet **1**: 992, 1938. Greenhill, J. P., and Freed, S. C.: Virilism in Women Caused by Androgenic Therapy for Menstrual Disorders, J. A. M. A. **112**: 1573 (April 22) 1939. Mazer, C., and Mazer, M.: Endocrinology **24**: 599, 1939. Geist, Salmon and Gaines.[14] Salmon, Geist, Gaines and Walter.[15] Salmon, Geist and Walter.[5] Salman.[7] Geist, Salmon, Gaines and Walter.[11] Huffman.[20]

the ovary and its hormone production, is approximately from 500 to 600 mg., administered during one cycle. The administration of androgens in excess of this amount results in the elicitation of arrhenomimetic phenomena, whereas smaller amounts (less than 250 mg.) cause neither suppressive nor arrhenomimetic effects. It is obvious that, to be of any practical value, androgens would have to exercise their therapeutic properties below the threshold for arrhenomimetic effects. Fortunately, this happens to be the case. Although during the course of our studies patients have been given doses in excess of 500 mg., and some as much as 1,800 mg. a month, with consequent development of hirsuties, voice changes and acne, this occurred before the threshold level for arrhenomimetic phenomena was clearly determined. Since then it has been our practice to keep the dosage below this level, and we were gratified to find that androgens have a therapeutic action in doses which are considerably below the threshold for arrhenomimetic phenomena.

ABNORMAL UTERINE BLEEDING

In the past three years several investigators have reported good therapeutic results in functional bleeding obtained with testosterone propionate.[13] We reported a series of 25 cases in 1938[14] and an augmented series, totaling 45 cases, in 1940.[15] The results in these cases were, on the whole, good as regards the control of the bleeding. Because of the fact that in a number of those cases large doses (350 to 1,000 mg. a month) were given, arrhenomimetic effects developed. In spite of the fact that the hypertrichosis and voice changes subsequently disappeared, the occurrence of these side effects is a serious objection to the use of androgens in gynecology. Fortunately, subsequent studies revealed the fact that functional menorrhagia could be controlled, in the majority of instances, with doses of testosterone propionate which are below the threshold for arrhenomimetic effects.

TABLE 1.—*Results in Thirty-Three Cases of Functional Bleeding with Subarrhenomimetic Doses of Testosterone Propionate (150 to 250 Mg. a Month)*

	Cases	Percentage
Primary results in 33 cases (during initial course of therapy)		
Normal menses	25	76
Moderate improvement	5	15
Failures	3	9
Late results in 30 cases		
Good therapeutic results without further treatment (periods of observation from 6 months to 3½ years)		60
Normal menses	15 cases, 50%	
Hypomenorrhea	2 cases, 7%	
Amenorrhea	1 case, 3%	
Moderate recurrence, 8 cases (within 3 to 6 months) (subsequently controlled with supplementary androgen therapy)		27
Complete recurrence, 4 cases (within 3 to 6 months)		13

The clinical results obtained in the series of cases with doses below the arrhenomimetic threshold are shown in table 1. In the majority of the latter group doses not exceeding 250 mg. a month were given. The primary as well as the later therapeutic results with this dosage are not quite as good as those obtained by us with larger doses.[2] Thus, there were only 6.6 per cent failures in a series of 45 cases, in the majority of which the larger doses were given, in contrast to 9 per cent failures and 13 per cent recurrences in the series of 33 cases in which the smaller (subarrhenomimetic) doses were given. The lower percentage of satisfactory therapeutic results obtained with the smaller doses is more than compensated for, however, by the absence of arrhenomimetic effects in these series.

TABLE 2.—*Results in Twenty-One Cases of Uterine Bleeding Associated with Fibroids*

	Cases	Percentage
Primary results		
Good therapeutic results	15	71
Moderate improvement	4	19
Failures	2	10
Late results (follow-up, 3 mo. to 4 yr. in 19 cases)		
Normal menses	7	37
Moderate recurrence (controlled with supplementary androgen therapy)	4	21
Complete recurrence (9 of these were subsequently operated on: 7 were found to have submucous fibroids; 2, adenomyosis)	8	42

Menometrorrhagia Associated with Fibroids.—The results in this series were not as satisfactory as in the functional group. The primary results were good in the majority; that is, while the patients were receiving the androgen therapy, or for a month thereafter, bleeding was either completely suppressed or was less copious and of shorter duration. Discontinuation of the androgens was followed by complete recurrence of severe bleeding in 48 per cent. The majority of these patients were subsequently found to have either submucous myomas or adenomyosis. Four patients with uterine fibroids (in whom hysterectomy was contraindicated because of cardiovascular disease) have been satisfactorily controlled with small doses of testosterone propionate and methyl testosterone for more than three years.

Limitations of Androgens in the Treatment of Menometrorrhagia.—The value of androgen therapy in the treatment of abnormal uterine bleeding has become more clearly defined since we have had the opportunity of studying its effects in a large series of cases and over a longer period of time. It is quite clear now that this therapy is most effective in the functional type of menorrhagia or menometrorrhagia occurring in women at the premenopausal age. Occasionally in such patients amenorrhea develops which may last for as long as six months or appear to be permanent. In younger women the results are somewhat less satisfactory, recurrence being more frequent. We have found it advisable to forestall recurrences by continuing androgen therapy in small doses for a period of several months after the establishment of normal menstruation. Usually 10 mg. of testosterone propionate, once or twice a week, is sufficient. We have found that oral (methyl testosterone) or sublingual (testosterone propionate in propylene glycol solution) administration serves satisfactorily as supplementary therapy. It is worth remembering that androgens have no cumulative effects as regards the arrhenomimetic phenomena. Apparently, if the hormone is given in small doses (e. g. from 10 to 20 mg. of testosterone propionate weekly, or from 5 to 10 mg. of methyl testosterone daily), it produces none of these effects even if it is continued for many

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15. Salmon, U. J.; Geist, S. H.; Gaines, J. A., and Walter, R. I.: Am. J. Obst. & Gynec. **41:** 991, 1941.

months. Some of the patients have received these small doses for periods of from six to sixteen months, totaling as much as 930 mg. of testosterone propionate and more than 2,000 mg. of methyl testosterone, without any arrhenomimetic effects or acne.

At this point, we think it important to point out that, although we believe that androgen therapy is effective in certain types of abnormal bleeding, one should not begin androgen therapy before definitely excluding neoplastic disease. It has been our practice to do either an endometrial biopsy or curettage in all cases prior to treatment.

FUNCTIONAL DYSMENORRHEA

Limitations of space do not permit a review of the theories of the etiology of functional dysmenorrhea.

The crux of the problem appears to lie in the fact that dysmenorrhea is not a clinicopathologic entity but rather a symptom complex which may be caused by a number of apparently unrelated factors, acting separately or in combination. In some cases, mechanical factors or intrauterine disease (adenomyosis), may be responsible for the symptoms. Furthermore, it is difficult to evaluate the role played by psychic factors both with regard to the causation of the symptoms and their amelioration. This probably accounts for the wide variety of therapeutic agents that have been found efficacious in the hands of different observers. . . . From all the evidence available, it seems that functional dysmenorrhea is caused by a disturbance in myometrial function which, in all probability, is the result of a lack of integration of the various hormonal factors that normally produce rhythmic painless contractions. Whether this is due to excessive estrogen and/or progesterone stimulation or to a disturbance of their physiologic interrelations, is, at present, not clear. But as a basis for understanding the therapeutic action of testosterone, it is sufficient if we accept the hypothesis that it is some aberration of gynecogen action on the myometrium that is the cause of functional dysmenorrhea. It has been shown that testosterone completely suppresses the contractions of the fallopian tubes [16] and uterus.[17] In smaller doses its suppressive effect is less intense and it probably reduces the excessive and abnormal uterine contractions to a physiologic pattern. Whether testosterone propionate accomplishes this by depressing the reactivity of the myometrium or by modifying or reducing the stimulating action of the estrogens remains, for the present, unknown.[7]

Dosage.—During the experimental stage of our study we treated dysmenorrhea patients with doses varying from 50 to 900 mg. a month, the total dosage varying from 100 to 1,500 mg. In our first series of 30 patients, reported in 1938,[3] the majority of the patients received more than 300 mg. a month; several received more than 600 mg. in one month. As a result of the high dosage employed, a number of characteristic arrhenomimetic effects developed. Since then, we have reduced the dosage below the arrhenomimetic threshold and have found that quite satisfactory therapeutic results can be obtained with doses not exceeding 250 mg. a month. Twenty-five mg. twice a week for the duration of one cycle was found sufficient in most instances. It is important not to discontinue the therapy completely as soon as the symptoms are relieved. The dose should be progressively reduced by approximately 25 per cent each month.

Results.—In the series of 30 cases reported in 1938 [3] there were 4 complete failures and in 4 only partial improvement; 22 cases, or 73 per cent, showed good primary results. Since then 25 more cases have come under treatment (with doses not exceeding 250 mg. a month), with essentially similar results (table 3). In 18 there was complete relief while under therapy; 4 showed considerable improvement and 3 no improvement. Of the 22 primary successes, 14 were kept on maintenance therapy for from two to three months after the initial course of treatment. This consisted, in the majority, of from 10 to 20 mg. of methyl testosterone, taken by mouth, for fourteen consecutive days, beginning on the twelfth day of the cycle. Twelve of these remained symptom free for periods varying from six to twenty months after discontinuation of the methyl testosterone. In 2 some recurrence of symptoms developed within three months after the methyl testosterone was stopped, with prompt relief after the medication was resumed.

In 8 of the cases with good primary results supplementary androgen therapy was not given. Of these, 5 remained symptom free for the period of observation, which varied from four to sixteen months. In 1 there was a moderate recurrence after four months; in 2, complete recurrence within three months after cessation of therapy. One of the latter was satisfactorily controlled with methyl testosterone. Further therapy was not attempted in the other because of an antecedent acne which seemed to be aggravated by the androgens. This case subsequently showed moderate improvement with ethinyl testosterone (pregneninolone).

TABLE 3.—*Results of Treatment in Twenty-Five Cases of Functional Dysmenorrhea with Subarrhenomimetic Doses of Testosterone Propionate*

	Cases	Percentage
Primary results		
Completely relieved	18	72
Considerably improved	4	16
Not improved	3	12
Late results in 22 cases with satisfactory primary results (4 to 20 months follow-up)		
(A) 14 with supplementary oral therapy (methyl testosterone) for 2 to 3 months		
12 symptom free for 6 to 20 months after discontinuation of oral therapy		
2 moderate recurrences within 3 months after discontinuation of oral therapy		
(B) 8 without supplementary therapy		
5 symptom free for 4 to 16 months		
1 moderate recurrence after 4 months		
2 complete recurrences within 3 months		

The recurrence of symptoms after discontinuation of the androgen and their prompt control with the resumption of androgen therapy suggests a replacement phenomenon. Of the 3 patients who were not improved, 2 had hypoplastic uteri and were subsequently treated with estrogens, with complete relief of the dysmenorrhea. The third had chronic adnexitis.

LIMITATIONS OF ANDROGEN THERAPY

The 4 failures in the first series of 30 cases and the 3 in the present series of 25 cases indicate the limitations of androgen therapy. Apparently, in the presence of endometriosis or chronic pelvic inflammatory disease, androgens have little effect in relieving the dysmenorrhea unless used in suppressive doses. The 2 cases of hypoplastic uteri which failed to respond to androgens but were relieved by estrogens point clearly to the advisability of giving estrogens from the beginning in such cases. The finding of a hypoplastic uterus in a patient complaining of dysmenorrhea should contraindicate the use of androgens.

16. Geist, S. H.; Mintz, M., and Salmon, U. J.: Proc. Soc. Exper. Biol. & Med. **41**: 556, 1939.

17. Robson, J. M.: Quart. J. Exper. Physiol. **26**: 355, 1937. Leonard, S. L.; Sager, V., and Hamilton, J. B.: Proc. Soc. Exper. Biol. & Med. **37**: 362, 1937.

It is worthy of note that none of the patients in this series showed hypertrichosis, changes in voice or enlargement of the clitoris.

PREMENSTRUAL TENSION

Premenstrual tension was first described by Frank[18] and attributed by him to hyperestrinemia with low excretion of estrogen. It has been suggested that the syndrome is the result of overstimulation of the autonomic nervous system by the gynecogens, namely the estrogens and/or progesterone.[19] On the basis of this theory, androgens have been used with gratifying results.[20] The emotional manifestations of this syndrome and the consequent difficulty of evaluating the role of psychogenic factors in the etiology of the disorder make it almost impossible to estimate the efficacy of the hormone therapy per se. However, the results of androgen therapy are so much more striking and uniform than other forms of treatment that we are inclined to the view that the relief of the symptoms is attributable to the androgens and not to incidental psychotherapy. Furthermore, 2 patients who were relieved with testosterone propionate were subsequently given, without their knowledge, progesterone for two consecutive cycles and, in both instances, the symptoms recurred.

Dosage.—We have found that 25 mg. twice a week, beginning on the twelfth day of the cycle and continued up to the next period, is sufficient in the majority of cases. Cases of severe involvement may require 25 mg. three times a week. The same course should be repeated for two additional cycles. Thereafter, the dose can be reduced to 10 mg. of testosterone propionate, twice a week, or 10 mg. of methyl testosterone a day for several cycles.

PREMENSTRUAL MASTOPATHIES

The premenstrual engorgement of the breasts which occurs normally in women has been shown to be caused by the stimulative effect of estrogens and progesterone on the epithelial elements of the acini and duct, as well as on the vascular elements.[21] When these phenomena become exaggerated, the result is extremely painful and tender breasts and nipples, frequently associated with tender "lumps." These clinical manifestations of hypergynecogen stimulation should respond to the antigynecogen property of androgens. The effectiveness of androgen therapy has been attested by the reports of several investigators. Good therapeutic results were first reported by Desmarest and Capitain[22] and have since been confirmed by others.[23]

Dosage.—Twenty-five mg. of testosterone propionate, twice a week, beginning on the twelfth day of the cycle and continued for two cycles, is usually adequate. Supplementary therapy with methyl testosterone (10 mg. daily, beginning on the twelfth day of the cycle) is recommended for several months after the discontinuation of the parenteral therapy.

POSTPARTUM PAINFUL ENGORGEMENT OF THE BREASTS

In women who do not wish to nurse, these unpleasant symptoms can be prevented by the postpartum administration of testosterone propionate.[24] We have obtained satisfactory results by administering 50 mg. of testosterone propionate intramuscularly within a few hours after delivery and 50 mg. daily for two days thereafter. One of us (U. J. S.) had the occasion to note recently, in 2 patients who decided to nurse their babies on the third and fourth days after they had received 150 and 250 mg. respectively, that, although the breasts were not tender or engorged, the patients were able to lactate adequately. We have found methyl testosterone, given orally, in doses of 60 mg. daily for four days as effective as testosterone propionate.

ENDOMETRIOSIS

The rationale for this treatment is based on the fact that the progress of the disease is predicated on the growth-stimulating effects of estrogens and progesterone on the ectopic endometrial tissue. Androgens have, therefore, been recommended in the treatment of the early stages of the disease and postoperatively in those cases in which the ovarian tissue is preserved because of the importance of conserving the reproductive function.[7] This therapy is manifestly not practical during the advanced stages of the disease. To be of any value, the hormone must be administered in suppressive doses and, in view of the fact that this approaches very closely the threshold for arrhenomimetic phenomena, the dosage should be carefully controlled with vaginal smears.

MENOPAUSE

The first report of the clinical use of androgens in the treatment of the menopausal syndrome was made by Mocquot and Moricard,[25] who described slight improvement in the flushes (with as little as a single injection of 5 mg.) but noted intensification of the nervous instability. It has been shown[1] that by administration of large doses of testosterone propionate (815 mg.), the gonadotropic hyperactivity of the hypophysis in a surgical castrate can be inhibited and the symptoms relieved. These clinical and hormonologic observations have since been confirmed.[26]

Unfortunately, the impression has been created by several clinical reports that testosterone propionate is as effective as estrogen in the treatment of the menopausal syndrome. This is not in agreement with our observations. It is true that in large doses (from 100 to 200 mg. a week, for several weeks), testosterone propionate has an estromimetic effect and can relieve the menopausal symptoms in a considerable number of cases. This is, however, a slow and expensive method of achieving a therapeutic effect which can be obtained more rapidly, completely and inexpensively with estrogens. There are, however, three groups of patients in whom androgen therapy is indicated for the menopausal syndrome: These are patients with menopausal symptoms who are still menstruating or have menorrhagia or metrorrhagia. Administration of estrogens to such

18. Frank, R. T.: Hormonal Causes of Premenstrual Tension, Arch. Neurol. & Psychiat. **26:** 1053 (Nov.) 1931.

19. Of considerable interest, in this connection, is the finding by Hamblen of excessive amounts of pregnandiol in a patient with this syndrome (Endocrinology **24:** 269, 1939). See also footnote 7.

20. Salmon, Geist and Walter.[3] Salmon.[7] Salmon, Geist, Gaines and Walter.[15]

21. Rosenberg, A.: Frankfurt Ztschr. f. Path. **27:** 466, 1922. Lewis, Dean, and Geschickter, C. F.: Am. J. Surg. **24:** 280, 1934.

22. Desmaret, E., and Capitain, Mme.: Presse méd. **45:** 777, 1937.

23. Douay, M.: Compt. rend. Soc. franç. de gynéc. **8:** 165, 1938. Huffman, J.: Am. J. Obst. & Gynec. **40:** 675, 1940. Loeser.[4] Salmon.[7]

24. Kurzrok, Raphael, and O'Connell, C. P.: Endocrinology **23:** 476, 1938. Birnberg, C. H.; Kurzrok, L., and Klor, S. J.: Am. J. Obst. & Gynec. **39:** 107, 1940. Salmon.[7] Geist.[4] Leonard, Sager and Hamilton.[17]

25. Mocquot, P., and Moricard, R.: Bull. Soc. de gynéc. et d'obst. **25:** 787, 1936.

26. Nathanson, I. T., and Towne, L. E.: Endocrinology **25:** 754, 1939. Birnberg, C.; Kurzrok, L., and Livingston, C., ibid. **23:** 243, 1938. Laroche, G.; Simonnet, H., and Bompard, E.: Compt. rend. Soc. de biol. **129:** 953, 1938.

patients not infrequently results in aggravation of the bleeding.[7] The second group consists of patients in whom the symptoms are only partially relieved by estrogens. These patients frequently respond to small doses of androgens (from 10 to 25 mg. a week) as a supplement to the estrogens.[7] A third group consists of postmenopausal patients who are distressed by the uterine bleeding resulting from estrogen therapy. In these patients, we have found that the combining of androgens with estrogens is effective in controlling the symptoms without inducing bleeding. The optimal ratio varies somewhat in different women. We have found that in the majority of these patients a ratio of estradiol to testosterone of 1 : 10 by weight (given parenterally) is satisfactory. We have found the vaginal smear useful as a guide in adjusting the ratio to individual needs.

VALUE OF VAGINAL SMEARS IN REGULATING ANDROGEN DOSAGE

During the course of our studies it was observed that the vaginal smears would frequently reveal signs of estrogen deficiency before any clinical evidence of overdosage was noted.[27] Making use of this observation, we have found it of value to take vaginal smears each week during the course of the androgen therapy. With the fuchsin stain [28] a smear can be stained and read in a few minutes. At the first sign of effect from the androgen in the vaginal smears, androgen therapy should be discontinued.

METHYL TESTOSTERONE

Methyl testosterone has been found to be a therapeutically effective androgen when administered by the oral route. Its biologic and therapeutic properties are similar to those of testosterone propionate.[7] Per unit of weight, it appears to be approximately one third to one half as effective by mouth as testosterone propionate is when administered parenterally. This compound is absorbed also in effective amounts when administered by inunction to the skin, but this method of therapy is unsatisfactory because of the difficulty in controlling the dose and the annoyance to the patient.

SUBLINGUAL ABSORPTION OF TESTOSTERONE IN PROPYLENE GLYCOL SOLUTION

We have found that estradiol [29] and testosterone [15] are absorbed in therapeutically effective amounts if administered sublingually in solution in propylene glycol. The androgen solution contains 25 mg. of testosterone per cubic centimeter of propylene glycol. In order to insure absorption of the hormone, the drops are instilled under the tongue and the patient is instructed not to swallow for five minutes. Preliminary studies have shown that this is an economical method of administering androgens. It is still, however, in an experimental stage.

IMPLANTATION OF CRYSTALS AND PELLETS OF TESTOSTERONE AND TESTOSTERONE PROPIONATE

Loeser [30] has reported satisfactory therapeutic results in 6 patients with menometrorrhagia (5 with fibroids; 1 with functional menometrorrhagia) and 2 with chronic cystic mastitis who were given implantations of testosterone and testosterone propionate. During the past three years, we have implanted crystals and pellets of testosterone and testosterone propionate in more than 40 patients in weights varying from 50 to 675 mg. We have found this method of administration of androgen of little value for clinical purposes. While there is no doubt that androgens administered by implantation are therapeutically effective, a number of the patients had arrhenomimetic symptoms within a few weeks, necessitating the excision of the pellets. In view of the proved effectiveness of parenteral and enteral administration of androgen and because of the importance of being able to vary the dose in accordance with the patient's response so that the maximum therapeutic effect is obtained without inducing the arrhenomimetic effects, it seems to us that there is hardly any justification for the implantation of androgen.

ETHINYL TESTOSTERONE (PREGNENINOLONE)

Ethinyl testosterone, which is closely related chemically to both progesterone and testosterone, possesses a unique variety of biologic properties. In animals, it has a progestomimetic, some estromimetic and very slight andromimetic action.[31] It is, furthermore, active when administered orally.

In a series of 28 cyclic women, treated orally with doses varying from 30 to 60 mg. a day over periods of from one to three months, none of the suppressive effects which can be so strikingly produced with testosterone propionate and methyl testosterone were observed. Menstruation was never suppressed and no estrogen deficiency phenomena appeared. Furthermore, in no instance did virilization phenomena develop.[32]

When administered orally to postmenopausal women, after adequate priming with estrogens, progestational changes were produced with doses of from 300 to 600 mg., administered over periods of from one to two weeks.[33]

In ethinyl testosterone there is available an orally active substance which has a progesterone-like action. We have found it helpful in some cases of dysmenorrhea and premenstrual tension.[7] It has proved ineffective, in our hands, in controlling functional menometrorrhagia.[34] Because of its progestomimetic action, this compound has been recommended in the treatment of threatened abortion.[35] Owing to the difficulty of evaluating its effectiveness, the use of ethinyl testosterone in this condition must still be considered as experimental.

COMMENT

The therapeutic effectiveness of androgens appears to stem from the the ability (*a*) to inhibit the gonadotropic activity of the hypophysis, (*b*) to suppress or decrease estrogen production, (*c*) to nullify or modify the activity of the gynecogens, (*d*) to inhibit the proliferative processess in the endometrium and (*e*) to inhibit the reactivity of the uterine musculature.

As one reviews the complex biologic properties of testosterone propionate one cannot avoid the implication that, in the normal human female, endogenous androgens may have a somewhat similar function to perform.

27. Salmon, Geist, Gaines and Walter.[18] Salmon, Geist and Walter.[3] Salmon.[7] Geist, Salmon, Gaines and Walter.[15]
28. Salmon, U. J., and Frank, R. T.: Proc. Soc. Exper. Biol. & Med. **33**: 612, 1936. Geist, S. H., and Salmon, U. J.: Am. J. Obst. & Gynec. **38**: 392, 1939.
29. Salmon, U. J., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. **45**: 766, 1940.
30. Loeser, A. A.: Brit. M. J. **1**: 479, 1940.
31. Salmon, U. J., and Salmon, A. A.: Proc. Soc. Exper. Biol. & Med. **43**: 709, 1940.
32. Salmon, U. J., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. **45**: 522, 1940.
33. Salmon, U. J.; Walter, R. I., and Geist, S. H.: Proc. Soc. Exper. Biol. & Med. **40**: 252, 1939.
34. Gaines, J. A.; Geist, S. H., and Salmon, U. J.: J. Clin. Endocrinol. **1**: 554, 1941.
35. Krohn, L., and Harris, J. M.: Am. J. Obst. & Gynec. **41**: 95, 1941.

There are a number of observations that support the theory that androgens play a physiologic role in the sex hormone organization of the human female. It has been shown that adult women excrete significant amounts of androgens [36] which are chemically identical with the androgens excreted by males, whereas the excretion of androgens before puberty and in old age is extremely small.[37] It may be inferred therefrom that androgens play some physiologic role in the sex hormone metabolism associated with menstruation. The demonstrated antigynecogenic properties of androgens in cyclic women and their therapeutic effectiveness in women presenting symptoms attributable to excessive or abnormal gynecogenic stimulation suggest that in normal women androgens have an antigynecogenic function; that normally the androgens and estrogens balance each other; that in certain gynecologic disorders the androgenic influence is defective or deficient (e. g., functional menorrhagia, dysmenorrhea, premenstrual tension) and that in others (e. g., amenorrhea, hypertrichosis) the androgenic influence is dominant. In the light of this theory, the use of androgens in gynecology can be considered as rational substitution therapy.

SUMMARY AND CONCLUSIONS

1. Four hundred and twenty-two women were treated with androgens during a period of five years.

2. Therapeutic effectiveness of androgens stems from their ability (*a*) to nullify or modify the action of estrogens, (*b*) to suppress or decrease the production of estrogens by the ovary, (*c*) to inhibit the proliferative processes in the endometrium, (*d*) to inhibit the reactivity of the uterine musculature and (*e*) to inhibit the gonadotropic activity of the hypophysis.

3. Doses of 500 mg. or more a month have a suppressive effect on the pituitary-ovarian-uterine system, suppressing gonadotropin production by the hypophysis, follicle growth and ovulation, and estrogen and progesterone formation, inducing involutional changes in the endometrium and vaginal mucosa. Doses of this magnitude may induce acne and arrhenomimetic effects, namely hypertrichosis, deepening of the voice and slight enlargement of the clitoris.

4. Androgens exert their therapeutic effects in subarrhenomimetic doses, namely less than 300 mg. a month.

5. Androgens have been found effective in the treatment of (*a*) functional menometrorrhagia, (*b*) functional dysmenorrhea, (*c*) premenstrual tension, (*d*) premenstrual mastopathies, (*e*) postpartum engorgement of the breasts and (*f*) certain types of the menopause syndrome.

6. Androgen therapy has been found of value in less than 50 per cent of the cases in which menometrorrhagia was associated with uterine fibroids. Androgens appear to be of no value if the abnormal bleeding is attributable to submucous myomas.

7. An orally effective androgen is available in the form of methyl testosterone. Testosterone has also been shown to be absorbed in effective amounts when administered sublingually in solution in propylene glycol.

8. Pellet implantations of androgens have been found to be therapeutically effective, but they are not recommended for clinical use because of the greater advantages of parenteral and oral therapy.

9. In the doses recommended, the danger of arrhenomimetic effects (hypertrichosis, deepening of the voice, enlargement of the clitoris) resulting from androgen therapy is practically negligible.

10. A theory is formulated of the physiologic role played by androgens in the sex-endocrine balance of the normal female. In the light of this theory, functional menorrhagia, dysmenorrhea and premenstrual tension may be regarded as manifestations of a disturbance of the androgen-gynecogen balance resulting in an abnormal dominance of the gynecogens. Administration of androgens, in order to restore the normal balance, would, accordingly, appear to be rational therapy.

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36. Womack, E. B., and Koch, F. C.: Endocrinology **16**: 273, 1932. Kenyon, A. T.; Gallagher, T. F.; Peterson, D. H.; Dorfman, R. I., and Koch, F. C.: J. Clin. Investigation **16**: 705, 1937. Koch, F. C., in Harvey Lectures, 1937-1938, Baltimore, Williams & Wilkins Company, 1938, p. 205. Butenandt, A., and Dannenbaum, H.: Ztschr. f. physiol. Chem. **229**: 192, 1934. Callow, N. H., and Callow, R. K.: Biochem. J. **32**: 1759, 1938. Hamblen, E. C.; Ross, R. A.; Cuyler, W. K.; Baptist, M., and Ashley, C.: Endocrinology **25**: 491, 1939. Hamblen, E. C.: J. Clin. Endocrinol. **1**: 180, 1941. Fraser, R. W.; Forbes, A. P.; Albright, Fuller; Sulkowitch, H., and Reifenstein, E. C., Jr., ibid. **1**: 234, 1941.

37. Oesting, R. B., and Webster, B.: Endocrinology **22**: 307, 1938. Nathanson, I. T.; Towne, L. E., and Aub, J. C., ibid. **24**: 335, 1939. Dorfman, R. I.; Greulich, W. W., and Solomon, C. I., ibid. **21**: 741, 1937.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. HAMBLEN AND DRS. GEIST AND SALMON

DR. CHARLES MAZER, Philadelphia: Dr. Geist and his associates attempt to formulate a theory as the basis for the marvelous results they obtained with the use of androgens in dysfunctional uterine bleeding, dysmenorrhea and premenstrual tension. They theorize that these three and almost all other dysfunctional gynecologic manifestations are due to a physiologic imbalance in the production of gynecogens and androgens. If this theory was correct, how could substitutive or complemental treatment with androgens relieve permanently so many of the patients? That androgens nullify or modify the activity of the gynecogens on the endometrium is evident from their ability to prevent estrogen-withdrawal bleeding in the castrated Rhesus monkey and human being. This local effect can be obtained in at least 50 per cent of menometrorrhagias of the dysfunctional type with the use of small doses of testosterone propionate, such as a total of 50 to 200 mg. There is, therefore, no need for the use of the large doses which inhibit, though temporarily, the pituitary ovarian mechanism and which are, moreover, too costly for the average patient. Even the smaller doses have, in my experience, evoked temporary masculinizing phenomena in 6 per cent of patients under 40 years of age. How distressing is even slight hypertrichosis to women at any age is well known. Fortunately, dysfunctional uterine bleeding occurring at this age can usually be controlled by other therapeutic measures which are less costly and less likely to produce undesirable by-effects. For these reasons it seems desirable to restrict, except in rare instances, the use of androgens to the premenopausal type of dysfunctional uterine bleeding wherein chorionic gonadotropin and other nonsurgical therapeutic agents are more or less ineffective. Premenopausal dysfunctional uterine bleeding, moreover, occurs at an age when suppression of the menstrual function merely hastens the inevitable and when temporary facial hairiness and hoarseness of the voice are more likely to be overlooked. In my experience both dysmenorrhea and premenstrual tension failed to respond to any appreciable degree to the administration of androgens in total doses of 50 to 200 mg. The remarkable results obtained by the authors with the use of the larger doses are noteworthy. Nevertheless, we must ponder whether these young women would not prefer their ailments to the risk of masculinizing effects, even if there were no other means of relieving their symptoms. The limited indications for estrogen therapy, as outlined by Dr. Hamblen, can be heartily endorsed. The substance has no peer in the realm

of pharmacology for relief of severe menopausal symptoms, if the dosage is initially adequate in quantity and frequency of administration.

DR. LUDWIG A. EMGE, San Francisco: The authors have discussed the relative merits of diametrically opposed methods of treatment of the disturbances of the female sex organs. Dr. Hamblen's topic deals with a method of treatment which has experienced the test of time and therefore can be more readily evaluated than that discussed by Drs. Geist and Salmon. There is no doubt in my mind that estrogenic therapy has an important place in therapeutics. There is, however, grave doubt that it will keep this place unless its use is rigidly governed by physiologic principles. This can be achieved only if the doctor will make an effort to learn to understand the pharmacologic as well as the chemical nature of estrogenic substances, relying more on his own efforts of observation and deduction than on those enthusiastic detail men. The estrogens essentially are of substitutional value. They do not stimulate the ovaries nor do they make better ovaries, and they are not a panacea for all the ills of womankind. All you can expect of them is to take over at least temporarily the duties of the follicular apparatus. They will not correct any progressive deterioration of ovarian function. Their action is purely substitutional as far as we know today. Withdrawal of treatment permits the return of deficiency phenomena; hence their use in the menopause warrants careful study. If, during the period of substitution, other endocrine glands resume a more normal function, resulting in improvement of the general physical state of a woman, it still does not mean that this becomes a permanent state. It therefore is imperative that the use of these substances is regulated by an intelligent application of physiologic principles. Any deviation from this rule debases this therapy to the level of quackery. There is no doubt that ovaries can be damaged, nor is there any doubt that other endocrines can be seriously disturbed. I agree with Dr. Hamblen that the usefulness of estrogens is limited and their use as tonics neither necessary nor economic. Drs. Geist and Salmon have acquainted you with a new therapeutic agent applicable essentially to the same group of disturbances discussed by Dr. Hamblen. Physiologically, the androgens oppose the estrogens and hence promise to be of great value when the action of the natural estrogens is out of control. Drs. Geist and Salmon's large series of observations strongly supports this assumption, and my own observations point in the same direction. However, I feel that the usefulness of the androgens also is limited. Time and usage are necessary to permit proper evaluation of these substances.

DR. JEAN PAUL PRATT, Detroit: The presentations by Drs. Geist and Salmon and by Dr. Hamblen represent two phases in the evolution of endocrine gynecology: the former, a period of experimental activity; the latter, a critical summary of previous experiments. The use of gonad materials to stimulate sex function goes back to antiquity. In 1849 the science of endocrinology began when Berthold demonstrated normal musculine development of castrated cocks by testicular grafts. In 1889 Brown-Séquard claimed sensational effects from testicular extracts administered to himself. In 1918 Pezard demonstrated development of the comb in capons by the injection of saline extracts of swine testes. Since 1927, when the first active principle of testes was isolated in Koch's laboratory, the field has widened rapidly. Androgens have been extracted from testes of animals and human urine. The chemical structure has been determined. Testosterone has been synthesized from cholesterol. Various compounds of the androgens have been prepared for experimental and clinical application. The effects in different species and in the human being have been compared. The effects at different ages and stages of development in both sexes have been studied. Today, Drs. Geist and Salmon have contributed an excellent comparison of several compounds. Many questions remain to be answered: What is the manner of action of the androgens? How are they utilized in the body? What is the effect on other endocrine glands and the whole organism? Why are androgens excreted in human urine but not in the urine of animals studied? What is the source of androgen in the female? It would seem that, with so many unanswered questions the study of androgens must be regarded as still in the experimental phase. Dr. Hamblen, in discussing the uses and limitation of estrogens in gynecic practice, is dealing with a much later phase in the evolution of endocrine gynecology. The estrogens have been widely used for many years. By the method of trial and error their limitations are now quite well defined. The story of ovarian therapy begins in 1898 with the assumption of Prenant that the corpus luteum looked like a gland of internal secretion. Therapy has run through the gamut of transplants, desiccated ovary, whole ovary, ovarian residue, all sorts of extracts to chemically pure sterols and finally to diethylstilbestrol, which is chemically unrelated to the estrogens but which has estrogenic action. The literature of the last four decades is replete with reports of successful therapy with each and all the numerous ovarian preparations. The success has been too often proportional to the enthusiasm of the patient and the doctor.

DR. JAMES B. HAMILTON, New Haven, Conn.: Male hormone substances (androgens) evoke definite responses in the female, and some of these actions have given rise to trial of their usefulness in gynecology. The problem at the moment, though, does not seem to be whether or not androgens evoke certain effects but whether they are the method of choice in management. That is a problem for the gynecologist. My associates and I have been studying the male eunuch and eunuchoid, particularly suitable subjects for study. They receive large doses for long-continued periods, as our desire is that which in the female would be excessive masculinization. With the use of these dosages in men previously lacking in androgens, we are in a position to look for extragenital effects. Of our series of patients, not one man requested treatment solely for any supposed enhancement of sexual capacity, but all state that they are benefited by the greater power of physical endurance. Vascular changes are characteristic, especially in the skin. The basal heart rate of the castrate is also increased when he receives androgens. McCullagh and Kenyon have shown that sufficient medication increases the basal metabolic rate and velocity of blood flow. These facts are mentioned, though they are not more significant than many of the other changes, such as the retention of salt, water and nitrogen described by Kenyon, Thorn and others. To some extent I must agree as to the obnoxious character of the temporary masculinization, but in these adult eunuchoids we have been able to obtain permanent masculinization with regard to only the lowering of the voice. That is the only change largely maintained for years after discontinuation of treatment. With the use of large doses, enlargement of the penis and of the genitalia occurs, but in our experience this tends to decrease after a while. We want to introduce a note of warning regarding the use of androgens in a woman who may be pregnant. This warning would apply also to the use of estrogens during possible pregnancy. Masculinization would not ensue, but there might be hypospadias, perhaps failure of testicular descent and a tendency toward development of female organs. There is indubitable evidence from animal experiments that pseudohermaphrodism can be and is produced by the influence of sex hormones at critical times during pregnancy.

DR. KARL JOHN KARNAKY, Houston, Texas: We have used androgens in several hundreds of cases in the Menstrual Disorder Clinic at the Jefferson Davis Hospital, Houston. We have used androgens routinely as advocated but have almost discontinued their uses entirely. Androgen is used occasionally in the menopausal patient. It was my good fortune to discover that diethylstilbestrol would stop functional uterine bleeding in five to thirty minutes when given in doses of 25 to 100 mg. into the anterior lip of the cervix. It was also discovered that diethylstilbestrol would cause atrophy of follicular cysts of the ovaries. In my opinion it is almost always retentive cysts of the ovaries that cause functional uterine bleeding, and diethylstilbestrol will eliminate the cause of the bleeding by causing follicular cysts to atrophy. Our clinic has studied more than 500 ovaries after giving androgen (testosterone proprionate) and diethylstilbestrol. After giving from 100 to 5,000 mg. of androgen we never could get complete atrophy of all the follicular cysts, while with diethylstilbestrol it required 100 mg. over a period of twenty days to eliminate completely all the

follicular cysts of the ovaries. Diethylstilbestrol has almost eliminated hysterectomies in cases of functional uterine bleeding. We have 700 cases of uterine bleeding in our series, in 500 of which we would previously have done a hysterectomy. We seldom do a hysterectomy just because of uterine bleeding. After more than 5,000 endometrial biopsies which were taken after all the way from 1 to 40,000 mg. of diethylstilbestrol had been given, estrogens, as far as we can observe, do not cause carcinoma. We have also shown that there is no such thing as a bleeding factor because we have produced uterine bleeding in children, and in women who have had radium or roentgen rays. Estrogenic hormones are apparently the bleeding factor.

DR. UDALL J. SALMON, New York: I regret that the impression has been created that androgen therapy in women inevitably results in the development of masculinization. This is an unfortunate misconception, since it creates an unjustified bias against a valuable therapeutic agent. We have treated more than 420 women with androgens for various gynecologic disorders and have encountered some degree of hypertrichosis or hoarseness in about 7 per cent of the cases. This includes those cases which were treated during the early experimental stage of this study, when we were interested in exploring the biologic properties of the androgens. With that end in view we had administered huge doses, in some instances more than 1,500 mg. during one month. Our studies have shown that there is a definite threshold for the induction of these masculinization phenomena, which is about 500 to 600 mg. of testosterone propionate a month. The therapeutic dose is very much below this, varying from 100 to a maximum of 300 mg. a month. There are, however, some individual variations in androgen susceptibility. Brunettes with a slight hypertrichosis appear to be the most susceptible. The average woman with no antecedent hirsuties can be safely given the therapeutic dose without fear of inducing hypertrichosis. We have found that frequently the smaller doses (100 to 200 mg. a month) will achieve satisfactory therapeutic results, particularly in cases of dysmenorrhea, premenstrual tension and mastalgia. With these smaller doses we have encountered no arrhenomimetic effects in over 200 cases. Furthermore, as regards avoiding these arrhenomimetic phenomena, there are certain morphologic signs which indicate androgen saturation. This is determined most simply by the vaginal smear, which can be prepared in a few minutes. The changes in the vaginal cells precede the appearance of the masculinization phenomena, so that the vaginal smears can serve as a simple method of guarding against overdosage. It is also worthy of note that the arrhenomimetic phenomena spontaneously regress after the discontinuation of the androgens. In regard to the danger of carcinogenesis resulting from estrogen therapy, Dr. Geist and I have conducted a study of this problem during the past six years on over 200 patients who had been treated with large doses of estrogens, and during the last two and one-half years on 180 patients who have been implanted with estrogen crystals and pellets. In these cases, periodic biopsies of the endometrium and vaginal mucosa failed to reveal any evidence of any atypical or neoplastic proliferation.

DR. SAMUEL H. GEIST, New York: The questions raised in the discussion are so numerous and so broad that it would be impossible in a short time to attempt even to touch on all of them. There is one thing that I wish to stress, which Dr. Pratt sensed immediately: this work as presented is experimental. After all, there must be some venturesome spirits among us if we are to establish facts therapeutic or physiologic; and we class ourselves as pioneers in this interesting field. It is only after a long series of experiments by many individuals over a period of many years that we shall be able to establish the fact that androgens have a definite place in the treatment of gynecologic disease. It is possible that they will not. Just as the limitations have been put on estrogens so aptly and so correctly by Dr. Hamblen, so shall we eventually be able to evaluate properly the use and therapeutic indication for androgens in gynecology.

DR. E. C. HAMBLEN, Durham, N. C.: There is only one comment which I should like to add: this is in regard to the so-called carcinogenic role of estrogens. Reference to possible carcinogenic effects by me was only for the purpose of repeating an old clinical warning. It is certain that, in clinical practice, natural estrogenic hormones have not been given, as yet, in such doses and over such periods of time to justify any serious anxiety in this regard. If some of the various estrogenic chemical substances of the diethylstilbestrol type, however, are made available in commerce, their unsupervised employment, i. e. in self medication, their high potency when taken orally and their cheapness may afford a closer approximation of the conditions which have characterized the production of carcinoma by estrogens in experimental animals. Under these circumstances a real danger may be recognized.

BRONCHIOGENIC CARCINOMA

INCIDENCE IN THE PACIFIC NORTHWEST, WITH A COMMENTARY ON EIGHTY-FOUR CASES

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Bronchiogenic carcinoma is so designated because of the widely accepted conviction that all primary pulmonary malignant neoplasms of epithelial origin arise from the bronchi or their accessory glands. Most introductory commentaries describe the investigator's interest as being aroused by his encountering an unusual number of cases of bronchiogenic carcinoma. Such experiences with this serious affliction, until recently regarded as extremely rare, have given impetus to numerous dissertations on the subject in many parts of the world.

In like manner, the abrupt appearance of primary cancer of the lung (in 1926) in our autopsy services aroused our interest, and in 1931 we [1] analyzed the basic pathologic, clinical and radiologic characteristics in 16 cases. Shortly thereafter a visit to the different institutes of pathology in Europe elicited, on inquiry, the interesting fact that the percentage of bronchiogenic carcinoma observed at autopsy was increasing in all these institutes.

The literature contains many contributions to the knowledge of the origin, nature and consequences of this form of cancer. Notable among these have been the monograph by Simons,[2] the symposium by Halpert [3] and the contributions by Ochsner and DeBakey.[4] The reader is referred to these for a complete review of the literature. However, there remains some question as to the relative or absolute increase of the incidence, the cause, the exact pathologic classifications and the concomitant symptoms. For this reason additional evidence is herewith presented.

INCIDENCE

Simons, after an extensive review, expressed the opinion that there was an increase both relative and absolute. This conclusion has been supported by many subsequent investigators. Rice [5] stated that there had been a decided increase in the last five years. Vinson [6] observed a well defined increase ("as frequent as pul-

The pathologists of the Northwest cooperated in this study.
From the Department of Pathology of the University of Oregon Medical School.
Read before the Section on Pathology and Physiology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Menne, F. R.; Bisaillon, Marr, and Robertson, T. D.: Northwest Med. **30**: 155 (April) 1931.
2. Simons, E. J.: Primary Carcinoma of the Lungs, Chicago, The Year Book Publishers, Inc., 1937.
3. Halpert, Bela: Surgery **8**: 903 (Dec.) 1940.
4. Ochsner, Alton, and DeBakey, Michael: Carcinoma of Lung, Surg. **42**: 209 (Feb.) 1941.
5. Rice, Carol M.: J. Lab. & Clin. Med. **21**: 906 (June) 1936.
6. Vinson, P. P.: Primary Malignant Disease of the Tracheobronchial Tree: Report of One Hundred and Forty Cases, J. A. M. A. **107**: 258 (July 25) 1936.

monary abscess") during the period 1925 to 1935. Rosedale and McKay [7] found bronchiogenic carcinoma to constitute 7.5 per cent of all carcinoma, being third in the list. Alwens and his associates [8] found a decided rise during the last ten years. Mattick and Burke [9] reported that at the Institute for the Study of Malignant Diseases, of 30,000 persons admitted, showing 18,000 malignant tumors, 73 (1 in every 250) had bronchiogenic carcinoma. This condition occurred with half the frequency of carcinoma of the stomach. A similar comparative observation was reported by Halpert.[3] Brines and Kenning [10] also stated that primary malignant tumor of the lung had developed from obscurity to importance, comprising 10 per cent of all cancer in Germany and being second to carcinoma of the stomach, as observed at autopsy in 3,000 cases. Cramer [11] quoted Peters as pointing out that the bronchiogenic type of neoplasm has advanced from fifth to second place and that in 1930 it constituted approximately 28.05 per cent of all carcinoma in men. Howes and Schenck [12] found 3 per cent of all carcinoma in the Brooklyn Cancer Institute to

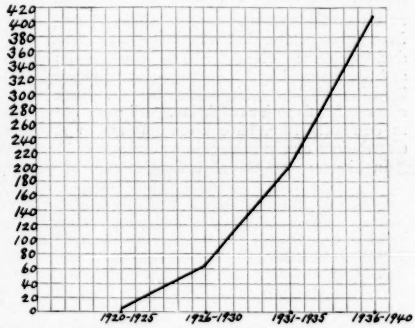

Fig. 1.—Composite curve illustrating the incidence of bronchiogenic carcinoma in the Northwest from 1920 to 1940, as observed at autopsy in 33,945 cases.

be bronchiogenic. Lockwood's [13] percentage was somewhat greater, being 6 to 8. Lockwood further noted that twenty years ago the condition was diagnosed in only 5 per cent of patients during life, while today it is recognized clinically in 50 per cent. It was his conclusion that carcinoma of the lung is on the increase in spite of the improved methods of diagnosis. A report [14] of the Chicago Tumor Institute for a period of two years revealed a smaller incidence of bronchiogenic carcinoma (1.14 per cent of all malignant tumors). Lovelock,[15] while undecided as to the relative or absolute increase, pointed out that European authors often have expressed the view that the increase is relative and not absolute.

Discordant opinions have been voiced by several authors. Stein and Joslin [16] expressed the belief that the increase is due to greater diagnostic accuracy but observed that there was a steady increase as compared with the incidence of carcinoma of the larynx and the lip from 1931 to 1936. Brunn [17] reported 488 instances in 192,271 necropsies (0.24 per cent) from 1898 to 1916. Jaffé [18] noted an incidence of 11.47 per cent of all carcinoma, as compared with one of 10.73 per cent observed in an earlier series of autopsies performed in Vienna (1915 to 1918) and concluded that the increase is more apparent than real. Boyd [19] pointed out that carcinoma of the lung is third in frequency, being exceeded only by carcinoma of the stomach and carcinoma of the large bowel. He recorded 53 instances among 4,500 autopsies (1.2 per cent) from 1925 to 1936 and 64 instances among 2,408 autopsies (2.6 per cent) from 1927 to 1937. This author commented that the worldwide character of the increased incidence has been "phenomenal . . . during the last twenty-five years." However, he concluded that the increase is more apparent than real and that it is due to the recognition of pulmonary carcinoma, the increased facilities for diagnosis and the increased number of autopsies. He further asserted that there was a parallelism between the increase of carcinoma of the lung and the increase of other diseases as revealed by vital statistics. He credited to the use of the bronchoscope and roentgen rays the earlier and more frequent recognition of bronchiogenic carcinoma. In addition, Boyd attributed to the inaccuracy of the differential diagnosis of certain types of bronchiogenic carcinoma from such conditions as Hodgkin's disease and lymphosarcoma a false increase in the incidence of carcinoma of the lung. Middleton [20] regarded the increased span of life and the "clinical and pathologic diagnostic consciousness" as being in part responsible for the apparent gross increase.

Our own experience in the study of the incidence of bronchiogenic carcinoma has been at variance with the conclusion that the increase is more apparent than real. Accordingly, it was decided to determine the occurrence of bronchiogenic carcinoma in the Pacific Northwest. We therefore sent a questionnaire to the members of the Pacific Northwest Society of Pathologists, requesting the incidence observed at autopsy. An analysis of the returns disclosed that from 1920 to November 1940, 33,945 postmortem examinations were made, revealing a total of 517 instances (1.52 per cent) of primary bronchiogenic carcinoma. Some of these were recognized by biopsy and others by combinations of clinical observations, biopsy and final autopsy. For recording the instances, the 20 years was divided into four five-year periods. During the first period, 1920 to 1925, only 3 instances were recorded, 1 at the University of Oregon Medical School (department of pathology) and 2 at the Good Samaritan Hospital. In the second period, 1926 to 1930, 63 cases were noted; from 1931 to 1935, 201, and from 1936 to 1940, 407. The striking increase in the last period as compared with that in the first is undoubtedly due in part to better diagnostic facilities and the presence of pathologists in institutions which had previously had none except in the Vancouver General Hospital, the University of Oregon Medical School and the Good Samaritan Hospital, where both diagnostic facilities and pathologists were available during the entire twenty years. It is significant, however, that during the last two periods, namely 1931 to 1935 and

7. Rosedale, R. S., and McKay, D. R.: Am. J. Cancer **26**: 493 (March) 1936.
8. Alwens, W.; Bauke, E. E., and Jonas, W.: München. med. Wchnschr. **83**: 485 (Nov. 8) 1936.
9. Mattick, W. L., and Burke, E. M.: Primary Bronchogenic Carcinoma from Pathologic and Radiologic Points of View. J. A. M. A. **109**: 2121 (Dec. 25) 1937.
10. Brines, O. A., and Kenning, J. C.: Am. J. Clin. Path. **7**: 120 (March) 1937.
11. Cramer, H.: Deutsche med. Wchnschr. **63**: 1259 (Aug. 13) 1937.
12. Howes, W. E., and Schenck, S. E.: Radiology **32**: 8 (Jan.) 1939.
13. Lockwood, I. H.: South. M. J. **32**: 30 (Jan.) 1939.
14. Report of the Chicago Tumor Institute, April 1, 1938 to March 31, 1940.
15. Lovelock, J. E.: Brit. M. J. **2**: 8 (July) 1939.
16. Stein, J. J., and Joslin, H. L.: Surg., Gynec. & Obst. **66**: 902 (May) 1938.
17. Brunn, H.: Primary Carcinoma of Lung, Arch. Surg. **12**: 406 (Jan., pt. 2) 1926.
18. Jaffé, R. H.: J. Lab. & Clin. Med. **20**: 1227 (Sept.) 1935.
19. Boyd, William: Tr. & Stud. Coll. Physicians, Philadelphia **6**: 317 (Feb.) 1939.
20. Middleton, W. S.: Southwestern Med. **24**: 287 (Sept.) 1940.

1936 to 1940, there was an astounding and sharp rise in the incidence. A composite curve (fig. 1) based on the number of carcinomas occurring in the respective five year periods reveals a striking continuous elevation. It has been argued that the greater knowledge of the disease, the increased facilities for diagnosis and the greater number of autopsies adequately explain the greater number of occurrences throughout the two later periods. To ascertain if this was true we compared the yearly percentage of bronchiogenic carcinoma with the number of autopsies in two of the institutions in which trained pathologists had been present during the twenty years and in which diagnostic facilities were standardized in accordance with the developments of the period. It will

In order to determine the accuracy or inaccuracy of the seemingly convincing data, a further analysis of the incidence was made (fig. 3), based on a segregation of the cases of bronchiogenic carcinoma (in the same two institutions) as observed at autopsy during a particular period, into groups of not less than 20.[21] From 1928 to 1933 there were performed at the University of Oregon Medical School 3,129 autopsies, disclosing 23 cases of bronchiogenic carcinoma (0.73 per cent); from 1934 to 1937 there were 2,820 autopsies, disclosing 26 cases (0.92 per cent), while from 1936 to November 1940 there were 2,022 autopsies, disclosing 34 cases (1.68 per cent). Comparatively, in the Vancouver General Hospital from 1928 to 1933 there were 2,111

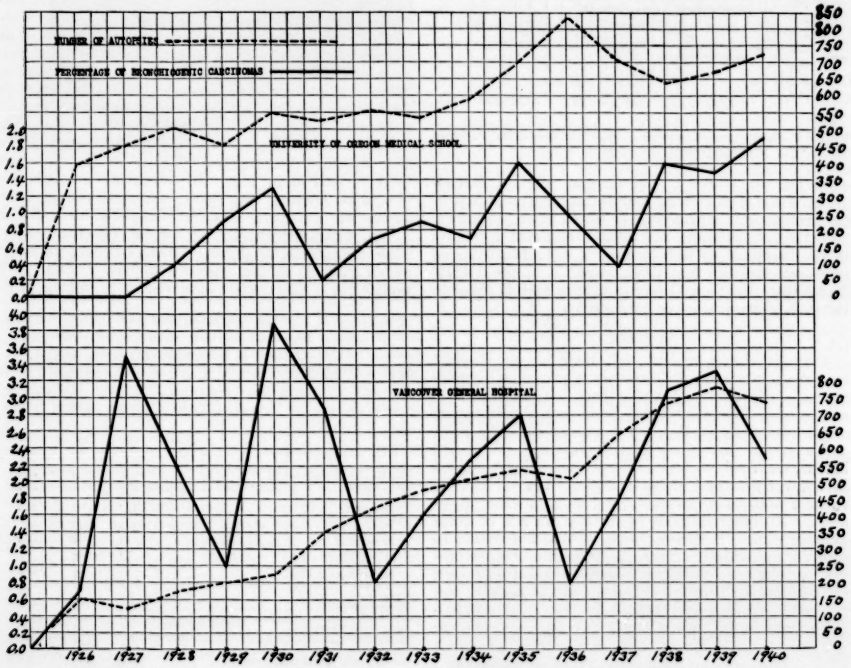

Fig. 2.—Relation of the incidence of bronchiogenic carcinoma to the number of autopsies performed from 1926 to 1940 inclusive.

be noted (fig. 2) that while there was a continuous, steady elevation in the number of autopsies performed throughout the years the percentage of bronchiogenic carcinoma did not parallel the increase in the number of autopsies for a given year and that not infrequently when there was a rise in the number of autopsies there was an actual decrease in the number of bronchiogenic carcinomas. It must be borne in mind that a rising total of autopsies also includes those performed on persons who have died from all causes. Epidemics of influenza or increased numbers of cases of pneumonia and other acute conditions may increase the number of deaths and the percentage of autopsies so that there may be an actual fall in the relative percentage of bronchiogenic carcinoma based on the total number of autopsies performed.

autopsies, disclosing 35 cases of bronchiogenic carcinoma (1.65 per cent), from 1934 to 1937, 2,206 autopsies and 40 cases (1.81 per cent), and in the final period (1938 to November 1940) 2,244 autopsies and 56 cases (2.49 per cent) (fig. 3). There is a striking parallelism in the incidence similar to that seen in figure 2.

The higher percentage at the Vancouver General Hospital in the periods stated may be attributed to less generalization in the performance of autopsies. That is to say, a greater percentage of autopsies may have been performed on all patients with bronchiogenic carcinoma, because of the unusual character of their disease, than

21. In determining the variations due to the laws of chance, as evidenced in a mathematical curve, a reasonably uniform number of not less than 20 must be selected. The greater the number in groupings of this kind, the more accurate is the percentage.

on patients with other conditions, whose death was not due to a malignant tumor. However, the number of cases during these periods at the Vancouver General Hospital was almost twice as great as that at the University of Oregon Medical School. By the same token, the percentage of error in estimating the incidence would be twice as accurate as that used in estimating the incidence at the University of Oregon Medical School. Since there is a striking parallelism, the accuracy of the incidence is enhanced. It would seem, therefore, from the preponderance of evidence submitted in reports in the literature as well as from a careful analysis of our own statistics and those available in the Pacific Northwest, that there is both a relative and an absolute increase of bronchiogenic carcinoma.

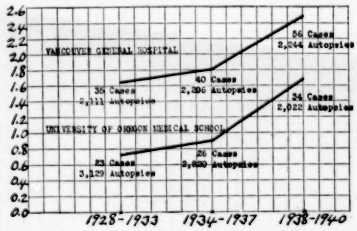

Fig. 3.—Relation of the incidence of bronchiogenic carcinoma to the number of autopsies performed in the University of Oregon Medical School and in the Vancouver General Hospital during three year periods.

ETIOLOGY

Since it seems evident that there is an absolute increase, the reason for it becomes of paramount importance. (See Simons [2] and others for detailed consideration.) The disease may be in such an early stage and so indefinite in its clinical aspects (Middleton [20]) as to escape detection until therapeutic procedures become extremely difficult. Even when it is recognized in the early stages, radical surgical removal has its dangers both as to mortality and as to altered physiology. All other methods of therapy are still of questionable value. It is accordingly of vital importance to consider the possible causes and to institute proper preventive measures. Unfortunately, study of our own series of cases as well as others yields nothing but speculative opinion as to the possible cause of bronchiogenic carcinoma. Much stress has been laid on the influence of prolonged and severe respiratory infections (e. g. influenza, pneumonia, tuberculosis) by Rice,[5] Vinson,[6] Brines and Kenning,[10] Cramer,[11] Turner and Willis,[22] Dressler and Weigl,[23] Kramer and Som,[24] and others. We also have been convinced that any continuous respiratory irritant or infection producing repeated denuding with reepithelization of the bronchial mucosa will either result or aid in the establishment of a malignant pattern.

Contamination of the air in areas of congested traffic and industry is receiving increased attention. Rosedale and McKay [7] and Dressler and Weigl [23] incriminated chromate dust as provocative in chemical industrial workers. Continued emphasis is being placed on the role of coal dust, chemical agents, radioactive substances and silicosis in mining and other industries (Charr,[25] Stein and Joslin,[16] Turner and Willis,[22] Lockwood,[13] Lovelock,[15] Lynch and Smith [26] and Dressler and Weigl [23]).

More recently investigators have turned their attention to the possible influence of the increased use of smoking tobacco (especially the marked increase in the use of cigarets). Myers [27] pointed to the enormous increase in the number of cigarets consumed in this country. In 1880, 582,718,995 cigarets were consumed, in comparison with 169,847,245,964 in 1937. Myers noted also that the toxic products of the combustion and distillation of tobacco are carbon monoxide, ammonia, formaldehyde, methylamine, methane, methyl alcohol, hydrogen sulfide, pyridine, furfural, arsenic and hydrocyanic acid. Of these the nicotine and tar contents are thought to be the most harmful. The former is an irritant of mucous membranes and the latter is regarded as carcinogenic. Myers [27] stated that "the smoking habits unquestionably increase the liability to cancer of the mouth, throat, esophagus, the larynx and the lungs." Cramer [11] noted that habitual smoking producing chronic inflammation of the mouth, pharynx, larynx and bronchial mucosa was present among the steel workers studied by him. In comparing the influence of tobacco smoking with that of the gases coming from automobile exhausts, Cramer [11] demonstrated that a 5 Gm. cigar yielded 200 mg. of tar (phenanthrene), while an eight hour drive 10 meters behind an automobile resulted in the collection of only 1.5 mg. of a similar tar. This author appeared to be convinced of the influence of tobacco smoking in the causation of bronchiogenic carcinoma. Roffo [28] stated that "the tobacco tars are very strong cancer producing" agents and that they are in the "same form as the coal tars and certain substances whose properties are very like those of the hydrocarbons distilled out of coal in their fluorescence and their spectrometry." He produced

Frequency of Various Symptoms and Signs with the Two Types of Bronchiogenic Carcinoma in Forty-Four of Fifty-Six Cases in Which Autopsy Was Done

Salient Symptoms	Group 1 (Carcinoma of Hilar Nodular Type) Number	Group 1 Percentage	Group 2 (Carcinoma of Diffuse Necrotic Type) Number	Group 2 Percentage
Cough	8	27.5	4	26.6
Cough with expectoration	19	65.5	9	60.0
Hemoptysis	14	48.2	3	20.0
Dyspnea	18	62.0	6	40.0
Cyanosis	4	13.7	2	13.3
Pain				
Mediastinal	6	20.6	0	0
Pleural	1	3.4	7	46.6
Intercostal	1	3.4	0	0
Unspecified	6	20.6	2	13.3
Other than in chest	7	24.1	1	6.6
Atelectasis	11	37.9	3	20.0
Empyema	2	6.9	1	6.6
Pleural effusion	5	17.2	5	33.3
Abscess of lung	5	17.2	3	20.0
Gangrene of lung	2	6.9	3	20.0
Hemothorax	0	0	3	20.0
Hoarseness	3	10.3	1	6.6
Cerebral and spinal symptoms	6	20.6	0	0
Ascites	1	3.4	0	0
Weakness and weight loss	8	27.5	3	20.0
Hemopericardium	1	3.4	0	0
Pancreatic fat necrosis	1	3.4	0	0
Lymphatic and venous obstruction	2	6.9	0	0
Total cases studied	29		15	
	44			

22. Turner, E. K., and Willis, R. A.: M. J. Australia **2:** 866 (Nov. 19) 1938.
23. Dressler, M., and Weigl, A.: Schweiz. med. Wchnschr. **69:** 763 (Aug. 26) 1939.
24. Kramer, R., and Som, M. L.: Bronchoscopic Study of Carcinoma of Lung, Arch. Otolaryng. **23:** 526 (May) 1936.
25. Charr, R.: Am. J. M. Sc. **194:** 535 (Oct.) 1937.
26. Lynch, K. M., and Smith, W. A.: Am. J. Cancer **36:** 567 (Aug.) 1939.
27. Myers, J. L.: Tr. Am. Laryng. A. **62:** 340, 1940.
28. Roffo, A. H.: Bol. Inst. de med. exper. para el estud. y trat. d. cáncer **15:** 406 (Sept.) 1938; cited by Myers.[27]

cancers by the application of tobacco tars to the ears of rabbits. He pointed out that "one can easily see large opportunity of cancerization in a regular smoker who consumes 1 kilogram of tobacco monthly, which means 70 cc. of tar." In this manner Roffo [28] reasoned that "the average smoker loads in one year 840 cc. and in ten years over 8 liters of tar on his buccopharyngo-

Fig. 4.—Encasement of the left primary and secondary bronchi by the new growth, hilar nodular bronchiogenic carcinoma.

laryngopulmonary membranes, which certainly have not the biologic resistance of the skin of a rabbit." Turner and Willis [22] observed bronchiogenic carcinoma in a gold miner who had influenza and smoked ½ pound (226 Gm.) of black tobacco a week.

Certainly the striking predominance of bronchiogenic carcinoma in men as compared with the incidence among women suggests either that in the industries men come in contact with an irritating substance or that the increased consumption (smoking) of tobacco by men as compared with its use by women is of great significance. It would seem that more careful recording of the histories to how much particular persons smoke would be of great value in determining the causal relation of the use of tobacco to bronchiogenic carcinoma. The average inquiry simply elicits information that the patient is or is not a user of tobacco. It is too early as yet to observe in the statistics of the literature the possible influence that tobacco smoking may exert on the incidence of bronchiogenic carcinoma in women, who are now smoking cigarets, often more excessively than do men. A report by Rice,[5] although it concerned a small number of patients (18 men and 12 women) seemed to indicate an increase among the women.

It seems obvious that the causative agent producing bronchiogenic carcinoma not only is air borne but is in a volatile state, since it involves the two lungs with almost equal frequency. Adequate information concerning correlative inflammatory phenomena in relation to the cause of bronchiogenic carcinoma is not at hand, since the average postmortem examination fails to comb completely the lung structure for initial lesions which might more accurately betray the influence of such phenomena. In the 4 instances of early bronchiogenic carcinoma to be reported by Hunter and his associates,[29] there were no clinical or gross pathologic evidences of such lesions. They were accidentally uncovered in the routine seelction of lung tissue for histologic study. Here then lies a field that needs more intensive tilling. At the time fully developed carcinoma of the lung is recognized there is considerable difficulty in defining cause and effect.

29. Hunter, W. C.: Unpublished data.

PATHOLOGY

In a previous communication we [1] discussed the extrinsic manifestations of the disease in relation to the existence of bronchiogenic carcinoma. At the time we pointed out that in 75 per cent of the instances there was bilateral chronic fibrous pleuritis indicating a previous inflammatory process of some moment. In addition there were acute empyema and other changes due to metastatic extensions in the mediastinum. In the majority of the instances the disease process had progressed so as to produce retraction of the mediastinal structures in the direction of the involved lung.

We were able to determine two more or less definite outstanding macroscopic types. One, in which the major lesions, at least in the less advanced stages, seemed to be that of maximum hilar accumulation, we designated the hilar nodular type; another, in which there was a diffuse involvement with a minimum of hilar concentration, was termed the diffuse necrotic type (figs. 4 and 5). Among 56 cases of bronchiogenic carcinoma in which autopsy was performed the carcinoma was of the hilar nodular type in 35 (62.5 per cent) and of the diffuse necrotic type in 21 (37.5 per cent). Regional pulmonary or lymphatic metastases occurred in all instances. Distant metastases were observed in 45. Whether this gross classification is of value may be open to question. Simons [2] quoted Aschoff as applying a macroscopic classification as follows: "(1) small nodular masses arising from bronchi of the first to the third order; (2) the infiltrating type in which a large portion of the lung or an entire lobe is involved." Rabin and Neuhof,[30] in a morphologic study of 100 cases (in which autopsy was done), divided bronchiogenic carcinoma into two main types, "circumscribed and noncircumscribed." The foregoing concepts of the pathologic classification of bronchiogenic carcinoma are similar to the one advanced by us in a previous communication.

Our studies led us to conclude that the majority of cancers of the lung arise in the primary and secondary

Fig. 5.—Diffuse character of the involvement of the lung; diffuse necrotic bronchiogenic carcinoma.

divisions of the bronchi. At autopsy confusion of growth and its consequences make localization difficult. Carcinoma of the so-called diffuse necrotic type in general arises in the more distal bronchi; however, variations in type are not entirely due to location but are in part patterns of a varied pathogenesis. Vinson [6]

30. Rabin, C. B., and Neuhof, H. A.: J. Thoracic Surg. 4: 147 (Dec.) 1934.

observed primary carcinoma in the trachea in 4 cases and in the bronchi in 87. Kramer and Som [24] concluded that 80 to 90 per cent originated in the bronchi, with 20 per cent of "parenchymal" origin. There is unanimity of opinion as to the more or less equal involvement of the lungs with a slightly increased incidence in the right (ratios given are, e. g., 6:4, 20:16 and 38:33). Of the 56 instances observed by us in detail, carcinoma was in the right lung in 28 and in the left in 27. Kramer and Som [24] in 100 postmortem examinations found the distribution of bronchiogenic carcinoma to be as follows: in the right lung—main bronchus 18, upper lobe 31, middle lobe 1 and lower lobe 12; in the left lung—main bronchus 8, upper lobe 17 and lower lobe 13. Carcinoma is observed in almost twice as many upper lobes as lower lobes. There is as yet no concrete evidence of bronchiogenic carcinoma's arising from atrial lining cells.

MICROSCOPIC STUDY

Many conflicting views are recorded as to the value and importance of histologic studies from both the academic and the practical point of view. Karsner and Saphir [31] expressed the opinion that the histologic classification of bronchiogenic carcinoma is the most satisfactory. The observations of Fried [32] with respect to the significance of the "reserve" cell type have permeated and influenced the considerations of the histology of bronchiogenic carcinoma. Practically all discussions confirm the existence of definite squamous cell types. The confusion of classification arises in proportion to the degree of anaplasia. Study of the cell structure of the tumors of 56 patients on whom autopsy was done revealed that 31 tumors were distinctly of the squamous cell type, with 9 disclosing keratinization, 15 showing no keratinization and 7 being distinctly anaplastic. Thirteen were found to be of the so-called adenocarcinomatous type, with only 2 showing mucus production. Eight were distinctly of the reserve cell type, 1 of the round cell type and 3 of the spindle or oat-shaped cell type. Again we wish to emphasize, as we did in our previous communication, that epithelial metaplasia with a subsequent malignant formation in the bronchi may result in all of the variable histologic types mentioned. We are of the opinion that with the so-called adenocarcinomatous type, except with growths arising from the mucous glands, the formation of acini is in part dependent on the structure of the lung and is more apparent than real. From the foregoing analysis it is obvious that the more or less confusing types of bronchiogenic carcinoma are decidedly in the minority. We refer in particular to the basal or reserve cell, round cell and spindle cell types. These constitute about 20 per cent of the total. There is, however, no particular confusion in recognizing the distinctly reserve cell type, so that there actually remains less than 1 per cent of primary carcinoma of the lung which may be confused with such lesions as lymphosarcoma. Vinson,[6] using the Broders method of grading, pointed to its advantage in the application of various kinds of therapeutic irradiation. He concluded that the so-called adenocarcinoma is the most radiosensitive.

PATHOGENESIS

The progressive and subsequent pathologic changes in bronchiogenic carcinoma are obviously primarily dependent on the status quo of lung structure, the bacterial flora and the site of the initial growth. When neoplasia originates in the primary or secondary bronchi, the direction of growth is, as we [1] have pointed out before, usually in the direction of the lumen. With the type designated by us as hilar nodular, analysis disclosed the sequence to be as follows: (1) hypertrophy, hyperplasia and metaplasia of the epithelium of the bronchus (carcinoma in situ); (2) partial or complete occlusion of the bronchus; (3) extension through the bronchial wall, with excitation of wandering cell infiltration and fibrosis; (4) further extension through the lymphatics; (5) involvement of the hilar lymph nodes, and (6) limited and slow massive extension into the lungs. With this type thromboses, coagulation necroses and secondary infectious processes are late in developing. The so-called diffuse necrotic type appears to us to be a manifestation of a more distant initiation in which the more delicate structure of the bronchus or bronchiole permits easier access to the surrounding lymphatics, with greater obstruction to the circulation. Primary carcinoma of this type appears to progress by (1) hypertrophy and hyperplasia of the epithelium (reserve cell type); (2) early extension into peribronchial lymphatics, with intrapulmonary lymphatic stasis; (3) engorgement and thrombosis of blood vessels; (4) secondary lobular pneumonic infection; (5) diffuse carcinosis; (6) coagulation necrosis with miliary abscess formation; (7) bronchiectasis limited to terminal bronchi, and (8) regional hilar node involvement, occurring in considerably less degree and later in the course of the disease. The carcinosis is characterized by spread through a definite lymphatic distribution in the lung as well as by continuity into tissue spaces. Pleurisy with effusion, because of extension to the pleura, is more frequent with this type. Furthermore, because of the earlier and more diffuse involvement of lymphatics and blood vessels, distant metastases (e. g. to the brain) are more common.

CLINICAL ASPECTS

No attempt will be made in this dissertation to analyze critically the various clinical concepts advanced in the literature by numerous writers. There is, however, universal agreement that the symptoms of bronchiogenic carcinoma are widespread and variable. Most writers on the subject agree that one must recognize two sets of symptoms and signs, those referable to the lungs and those arising from metastases in organs and tissues outside the chest. In our previous communication we attempted to correlate the symptoms, signs and radiologic data characteristic of bronchiogenic carcinoma in general and specifically of two more or less distinctive types (hilar nodular and diffuse necrotic).

In the present series of 84 cases, the average age was 55½ years, with a range of 38 to 77 years. In 78 cases the disease occurred in men and in 6 in women (13 to 1). These data are in agreement with those of the majority of reports. In a number of our cases adequate clinical data were not available, but in 44 of the 56 cases in which autopsy was done they were sufficiently complete to permit comparative evaluation of the signs and symptoms. In 29 of the 44 the carcinoma was of the hilar nodular type, and in 15 it was of the diffuse necrotic type (see accompanying table). An analysis of the salient symptoms and signs disclosed that cough with expectoration was the most frequent symptom, occurring in two thirds of the cases of both types of carcinoma. This was associated with hemoptysis in approximately half of the patients with hilar nodular

31. Karsner, H. T., and Saphir, Otto: Am. J. Path. 6: 553 (Sept.) 1930.
32. Fried, B. M.: Primary Carcinoma of the Lung, Baltimore, Williams & Wilkins Company, 1932.

carcinoma (group 1) but in only 20 per cent of the patients with diffuse necrotic carcinoma (group 2). Dyspnea was the second most common symptom. It was especially severe in group 1 (occurring in 60 per cent) and less pronounced in group 2 (occurring in 40 per cent). Cyanosis was present in 13 per cent of the patients and was frequently stated to be a terminal event. The time and location of the pain were significant in that 20 per cent of the patients of group 1 complained of mediastinal pain characterized as dull, substernal and deep seated. This pain was not present in group 2, but the majority of patients in this group evidenced pleural pain, indicative of metastatic or inflammatory involvement of the pleura. The third type of pain in the chest, which is frequently credited to involvement of the intercostal nerves or roots, was present in only 1 patient of group 1.

In 8 instances the type of pain in the chest was unspecified, and in an equal number pain occurred in locations other than the chest. The pain in all 16 was due to metastatic involvement of organs and tissues evidencing distress.

A significant condition definitely related to the pathogenesis was atelectasis in 38 per cent of the patients with the hilar nodular type (group 1) and in 20 per cent of those with the diffuse necrotic type (group 2). Empyema, pulmonary abscess and gangrene, which are complications due to the extension of the growth and are evidences of secondary infection, tended to be more frequent in the patients of group 2. Hemothorax, in our series, occurred only in patients of group 2 (20 per cent). Hoarseness, stated to be a frequent complication of mediastinal extension, was present in 10 per cent of group 1 and in only 1 patient of group 2. Weakness and loss of weight were common complaints in both groups.

In summary, it may be pointed out that approximately half the patients with hilar nodular carcinoma presented symptoms referable primarily to the lungs, while an equal number had symptoms attributable to metastasis. On the other hand, of the patients with diffuse necrotic carcinoma twice as many had symptoms traceable to metastasis as had symptoms referable to the lungs. It is apparent that symptoms originating in the lungs, such as cough, expectoration and dyspnea, occur more frequently in the earlier stages of the disease and are more common in patients with hilar nodular carcinoma. Conversely, the symptoms and signs resulting from pleurisy, pulmonary abscess, empyema, hemorrhage, dyspnea, cough, hoarseness, aphonia and neurotic involvement are more frequent with diffuse necrotic carcinoma. Apparently the last six symptoms are due to the earlier tendency to metastasize as well as to the earlier obstruction of smaller pulmonary units and their surrounding lymphatics and blood vessels. While there may be some criticism as to the feasibility of the clinical and pathologic division of bronchiogenic carcinoma into the types described, it seems to us that the variability of the initial site of bronchiogenic carcinoma may be expected to and does result in fundamentally different clinical and pathologic pulmonary carcinomatous lesions.

SUMMARY

1. Bronchiogenic carcinoma was observed 517 times during a series of 33,945 autopsies performed in the Pacific Northwest.

2. Statistical analysis based on the number of autopsies, time periods and chance variations indicate an absolute increase in the incidence of primary pulmonary carcinoma in recent years.

3. Emphasis is laid on the etiologic significance of inflammatory processes augmented by volatile irritants, such as tobacco smoke and gaseous products of the industries.

4. Eighty-four instances of bronchiogenic carcinoma were observed in the department of pathology; 78 of the patients were men and 16 women; autopsy was performed in 56 cases.

5. Bronchiogenic carcinomas are classified macroscopically into two types, hilar nodular and diffuse necrotic.

6. Histologic examination of the neoplasm in the 56 cases in which autopsy was done revealed that in 31 it was squamous cell carcinoma, in 13 so-called adenocarcinoma and in 12 reserve cell carcinoma.

ABSTRACT OF DISCUSSION

DR. HOWARD T. KARSNER, Cleveland: Although not always evident, there is value in analysis of the geographic distribution of disease. Climatic, occupational and perhaps dietary and other factors may be different in some respects in the Pacific Northwest from those which prevail elsewhere. It is therefore of interest to learn that bronchiogenic carcinoma is as common in that region as it is in other parts of the country. The authors review again the discussion concerning an increased incidence of this disease. There can be no doubt of a relative increase, but there may well be some question as to absolute increase. The population of the autopsy room is different from the living population, because it is a population determined by numerous factors of opportunity and interest. In ten years at the Cleveland City Hospital, 1927 to 1937 inclusive, bronchiogenic carcinoma constituted 9.4 per cent of all cases of malignant tumor examined at autopsy. No one would claim that about 1 of 10 living patients with malignant tumors has bronchiogenic carcinoma. If autopsy statistics were a guide in this connection it could be said that carcinoma of the lung arising in an obsolete primary tuberculous focus is on the increase because we have seen 3 such instances in the last year as compared with none in the preceding ten years. It is difficult to employ statistical analyses in determining absolute increase because there is no certain way to provide mathematical corrections that would fully account for improved diagnosis, special attention to the lesion, accurate interpretations of roentgenograms and precision of bronchoscopic examinations and biopsy. Nor are the errors inherent in the improved methods fully evaluated. For example, we have seen within a period of six months pneumonectomy in 2 cases not suitable for biopsy through the bronchoscope but characteristic in every way of bronchiogenic carcinoma. One was metastatic from a thyroid carcinoma treated surgically twenty years before and the other metastatic from an unnoticed malignant granulosa cell tumor of the ovary. No formula has yet been devised that meets all the factors of error, largely because these factors are not yet calculable. An absolute increase cannot be denied, nor is it fully established. The influence of various factors supposed to be responsible for an absolute increase is still in doubt. There is certainly no proved connection with epidemics of influenza, nor is there any frequency of association with pulmonary tuberculosis. Silicosis may be of importance but accounts for relatively few cases. Whatever accounts for the Joachimsthal cases does not prevail widely. If tobacco smoking were of significance, there should be an increasing incidence in women.

DR. BÉLA HALPERT, New Orleans: The contribution of Dr. Menne and Dr. Anderson presents evidence that there is a relative as well as an absolute increase in carcinoma of the lung. Their data from the Pacific Northwest on necropsy material are almost identical with those reported by Rosahn from the East and with our own data from the South. Carcinoma of the lung, in fact, is becoming the second if not the first most common malignant neoplasm in the male. Chronic irritations from infections, inhalation of gases, foreign bodies and

particularly smoking of tobacco with its nicotine and tar content may play a part, but perhaps more important is the fact that more people are reaching the cancer age. Whether the gross morphologic classification according to location and extent of the growth as suggested by Dr. Menne and the one by Dr. Karsner have any practical value remains to be seen. At present there are no gross criteria by which the cellular structure can be ascertained without microscopic examination. In looking for effective therapy the cellular structure is a decisive factor. It seems certain that successful radiotherapy of carcinoma of the lung is as yet impracticable. So, for the present, the only effective treatment is early recognition and, as suggested by Graham, Rienhoff, Overholt, Ochsner and DeBakey, Churchill and others, surgical removal of the involved lung—pneumonectomy.

DR. L. WALLACE FRANK, Louisville, Ky.: In my intern days, over twenty-five years ago, cancer of the lung was rare. Today it is exceedingly common. About four years ago I came to the conclusion that the probable cause of the increase of pulmonary cancer was related to the rapid increase in the number of automobiles and the increased use of tarred roads. I intended to work out a series of experiments to prove whether or not this was so but in studying the literature found that Campbell of England had already done the work. He studied mice, in which the known incidence of pulmonary carcinoma was 14 per cent. He took one group as controls and over the others blew twice daily the dust and scrapings from the roadways, most of which were made of some tar preparation. The incidence of pulmonary carcinoma in the second group was 76 per cent, compared with 14 per cent in the controls. I am of the opinion that Campbell's studies throw a great deal of light on the cause of the increase of pulmonary cancer.

DR. ISRAEL DAVIDSOHN, Chicago: When one evaluates all the factors which might have some significance in connection with the question of the absolute or relative increase of carcinoma of the bronchi, it seems worth while to point out the fact that until about 1926 the type of bronchiogenic carcinoma now referred to as reserved cell carcinoma was frequently mistaken for a primary sarcomatous growth of the lymph nodes in the mediastinum. The recognition of the true histogenesis of this tumor must of necessity influence the statistics of bronchiogenic carcinoma. I should like to ask the authors whether they have separated in their series the apical carcinoma originating in the peripheral bronchi, which, owing to its invasion of the bones in the region of the upper thoracic aperture and of the nerves, produces a very characteristic clinical picture (the so-called superior pulmonary sulcus tumor of Pancoast).

DR. FRANK R. MENNE, Portland, Ore.: As far as Pancoast's tumor is concerned, we did not encounter it. We have some papillary carcinomas occurring in association with apical scars that will be reported subsequently. I appreciate that several classifications of carcinoma of the lung have been advanced. Of course, when one deals with statistics one gets into trouble. I want to emphasize, however, again the fact that bronchiogenic carcinoma seems to me to be present out of all proportion to our increased knowledge, either clinically or pathologically, of this incidence, irrespective of the locality. I want also again to emphasize the fact that those carcinomas of the lung that are confused with primary tumors of the lymph in the lymph nodes or the lymphocytes or Hodgkin's disease are a small percentage of the bronchiogenic carcinomas that have been present in our experience.

Lazy Medicine.—That sort of medicine is lazy medicine. It is easier to get the answer out of a machine or out of laboratory reports than to sit down and think for yourself. Or at least the users of the machine think it is. In any event, it satisfactorily puts off until tomorrow, and perhaps forever, the examination you don't want to make today. The machine is made a substitute for thought. Unfortunately it is not invariably the correct answer which comes out; sometimes the machine speaks with the guile of the Delphic oracle, though the hearer does not realize it. And machine medicine may be not only lazy medicine, it may be dishonest medicine.—Atkinson, Miles: Behind the Mask of Medicine, New York, Charles Scribner's Sons, 1941.

NORMAL AND ABNORMAL BACTERIAL FLORA OF THE NOSE

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The frequency with which an abnormal bacterial flora was found in cases of frank nasal infection and in the nasal passages of persons without objective changes in the nasal mucosa or subjective symptoms of sinus infection led us to undertake a systematic and comprehensive study of the bacteriology of the nose.

METHODS

The nasal secretion of 500 consecutive patients admitted to our general medical service was cultured. The age of the patients varied from 4 weeks to 78 years. Cultures were made by inserting a sterile swab far back into the nasal cavity and streaking a blood (sheep blood) agar plate directly. Material from each side of the nose was cultured separately. In some cases cultures were made in the same manner with Löffler's medium. Cultures were made of sterilely obtained antral washings by inoculating nutrient broth, dextrose broth and blood agar plates. Cultures thus obtained were incubated at 37.5 C. for twelve to twenty-four hours, and the organisms were then identified by the appearance of the colonies, appropriate staining procedures and bile solubility tests. In many instances, cultures were made repeatedly during the initial hospitalization, return visits of outpatients or readmission.

RESULTS

The organisms found in the nasal passages varied considerably except for the constant presence of Staphylococcus albus and diphtheroid bacilli (table 1).

In every instance except 2 in which organisms other than staphylococci, diphtheroid bacilli and Micrococcus catarrhalis were isolated on culture from the nasal passages, abnormal changes or conditions existed in the nasal cavity and/or the paranasal sinuses. The 2 exceptions were the only instances in which green-forming streptococci were isolated from the nasal passages and could not be found on repetition of the culture. No abnormalities were demonstrable either clinically in the nasal cavity or by roentgenogram in the paranasal sinuses in these 2 cases. On the other hand, staphylococci and diphtheroid bacilli were found on culture in every case, whether or not there were objective changes in the nasal passages or the paranasal sinuses. Cultures of nasal secretion taken from patients with the "common cold" or an increased nasal discharge from any cause always showed an increase in the number of colonies of staphylococci and diphtheroid bacilli, regardless of what other organisms, if any, might be present. Children with the "common cold" frequently had pneumococci in the culture.

The organisms cultured from material from the nasal passages (other than staphylococci, diphtheroid bacilli and M. catarrhalis) were associated with many varied abnormalities of the upper respiratory tract. Sinusitis of the acute purulent, chronic purulent or chronic hyperplastic (nonpurulent) type was the condition most frequently encountered. The cultures of nasal secretion (tables 2, 3 and 4) most frequently showed green-forming streptococci, pneumococci or hemolytic strepto-

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cocci. Pneumococci and hemolytic streptococci were found most often in cases of acute sinusitis and green-forming streptococci in cases of chronic sinusitis. In approximately 20 cases green-forming streptococci were recovered from the nasal passages although clinical evidence of sinusitis and frank changes in the nasal mucosa were absent. However, in these cases nonsuppurative (hyperplastic) maxillary sinusitis was shown by roentgen examination. In a few instances green-forming streptococci were recovered from only one nasal passage, with roentgen evidence of sinusitis on the same side.

Hemolytic streptococci were cultured from material from the nasal passages in 15 of the 19 cases of scarlet fever, and occasionally green-forming streptococci were found. Pneumococci were cultured in 2 cases of lobar pneumonia, in one of which there was purulent pansinusitis. Likewise, diphtheria bacilli were cultured from the nasal secretion of 1 patient with clinically diagnosed pharyngeal diphtheria and from that of a diphtheria carrier who had chronic suppurative sinusitis. The latter had, in addition, both green-forming streptococci and hemolytic streptococci in the culture. Bacillus mucosus was found on culture in 2 cases of chronic atrophic rhinitis. In 1 of these hemolytic streptococci and pneumococci were also present, and in the other, hemolytic streptococci, diphtheria bacilli and green-forming streptococci. Both patients had a chronic form of maxillary sinusitis. Pfeiffer's bacillus was isolated from the nose in 1 case of clinically diagnosed influenza. Other conditions or lesions in association with which such organisms were found were nasal obstruction due to a markedly deviated septum, with reddened, wet mucous membranes; septal abrasions, and ulcers.

TABLE 1.—*Frequency of Various Organisms in Cultures of Nasal Secretion of Five Hundred Patients*

Organism	Occurrence	Percentage
Staphylococcus albus	500	100
Diphtheroid bacillus	500	100
Green-forming streptococcus	104	20 8.
Staphylococcus aureus	...	....
Hemolytic streptococcus	36	7.2
Pneumococcus	35	7.0
Micrococcus catarrhalis	..	...
Bacillus mucosus	6	1.2
Diphtheria bacillus	3	0.6
Pfeiffer's bacillus	2	0.4

TABLE 2.—*Abnormal Nasal Flora and Roentgen Evidence of Sinus Disease*

Patients with one or a combination of the following organisms in the culture: hemolytic streptococci, green-forming streptococci, pneumococci, diphtheria bacilli, Pfeiffer's bacilli, Bacillus mucosus	161
Number of roentgenograms of paranasal sinuses	90
Number of rentgenograms showing evidence of sinusitis	58
Percentage showing sinusitis	60.44

Green-forming streptococci or pneumococci were isolated from the antral washings of a number of patients who showed clinical and roentgen evidence of sinusitis.

COMMENT AND REVIEW OF THE LITERATURE

Bacteriology of the Nose.—The flora of the nasal passages has been studied by many observers. In 1898 Park and Wright [1] reported that the normal nose is not usually sterile but that organisms such as pneumococci and streptococci are rarely found. Neumann [2] in 1902 studied the nasal flora of more than 200 persons, 111 of whom were supposedly normal, with the results shown in table 5.

None of the patients in Neumann's study had roentgenograms of the paranasal sinuses made.

TABLE 3.—*Normal Nasal Flora and Roentgen Evidence of Sinus Disease*

Number of patients with normal nasal flora	339
Number of roentgenograms of paranasal sinuses	181
Number of roentgenograms showing evidence of sinusitis	20
Percentage showing sinusitis	11

TABLE 4.—*Frequency of Organisms in Cases of Roentgenologically Proved Sinusitis in Association with an Abnormal Nasal Flora*

Number of cases of an abnormal flora plus roentgen evidence of sinusitis	58
Number of cases in which there were green-forming streptococci	45, or 77.56%
Number in which pneumococci were found on culture of nasal secretion	9, or 15.51%
Number in which hemolytic streptococci were found on culture of nasal secretion	4, or 6.8%

Bloomfield [3] found that Staph. albus was present in every culture of nasal secretion and regarded its presence as a normal condition. Less frequently he found diphtheroid bacilli and Staphylococcus aureus and considered gram-negative cocci, B. lactis aerogenes and hemolytic streptococci to be transient forms. This view was held essentially by Noble and Fisher [4] and by Noble and Brainard.[5] They concluded that organisms such as hemolytic streptococci, green-forming streptococci and pneumococci, of known potential pathogenicity, are clinically significant only in the presence of a definite lesion in the nasal cavity but in the absence of a clinical lesion may be considered transients. According to our experience, whenever these organisms can be cultured from material from the nasal passages, changes in the nasal mucosa or secretion or in the paranasal sinuses are present. Webster and Hughes,[6] in a study of the epidemiology of pneumococcic infection, expressed the belief that persons from whom pneumococci could be constantly recovered were infected persons in the sense that the organisms were growing in the rhinopharyngeal tissues. These chronic carriers, according to their report, were not given a roentgen examination to determine whether paranasal sinusitis might have accounted for the repeated positive cultures.

Neufeld and Etinger,[7] in a study on children (aged 1 to 20 months) with acute coryza, found pneumococci in 65 per cent of cultures of nasal secretion. Our observation on children was similar except that pneumococci were found more frequently than green-forming streptococci when there was evidence of an infection of the upper respiratory tract. Shibley, Hanger and

1. Park, W. H., and Wright, J.: Nasal Bacteria in Health, New York M. J. **67**: 178 (Feb. 5) 1898.

2. Neumann, R. C.: Bakteriologische Untersuchungen gesunder und kranker Nasen, mit besonderer Berücksichtigung des Pseudodiphtheriebacillus, Ztschr. f. Hyg. **40**: 33, 1902.

3. Bloomfield, A. L.: Localization of Bacteria in Upper Air Passages, Bull. Johns Hopkins Hosp. **32**: 290 (Sept.) 1921.

4. Noble, W. C., Jr., and Fisher, E. A., and Brainard, D. H.: Studies of Acute Respiratory Infections, J. Prevent. Med. **2**: 105 (March) 1928.

5. Noble, W. C., Jr., and Brainard, D. H.: Bacteriology, J. Lab. & Clin. Med. **17**: 573 (March) 1932.

6. Webster, L. T., and Hughes, T. P.: The Epidemiology of Pneumococcus Infection, J. Exper. Med. **53**: 535 (Jan.) 1931.

7. Neufeld, F., and Etinger, R.: Pneumokokken in Nase und Rachen, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 2, pp. 885-891.

Dochez [8] studied 13 adults between October and June, making cultures of material from the nose and throat weekly when the person was in normal health and daily when a cold occurred. Their observations on the normal nasal flora agree essentially with those of the authors previously cited as well as with our own with respect to the frequency of staphylococci and diphtheroid bacilli. They concluded that gram-negative cocci and nonhemolytic streptococci are occasional transients in the nose but that in the presence of colds hemolytic streptococci and Pfeiffer's bacilli are frequently found. In our series green-forming streptococci and pneumococci were found during colds as frequently as hemolytic streptococci and more frequently than Pfeiffer's bacillus. Wirth and Braun [9] studied the bacteriology of the nose and throat during acute infections of the upper respiratory tract and concluded that the nasal passages assume a sympathetic role to one another, especially when hemolytic streptococci, pneumococci and influenza bacilli are the causative organisms. This conclusion came as a result of finding the organisms on culture of material from both sites so frequently. Wirth's [10] observations agree essentially with this observation, if one assumes that examination of the nasal bacteria was the easiest method of determining the causative agent of infections of the ear and the upper respiratory tract.

TABLE 5.—*Nasal Flora of Two Hundred Persons (Neumann [2])*

Organism	Percentage
Staphylococcus albus	98
Staphylococcus aureus	30
Streptococcus lanceolatus	4
Friedländer's bacillus	6
Micrococcus citreus	12
Escherichia coli	12
Streptococcus	2
Molds	20
Sarcina	4
Bacillus lactis aerogenes	4
Yeasts	2

In isolated instances other organisms have been found in cultures of nasal secretion. Meyer and Steenert [11] isolated the tubercle bacillus from the purulent nasal discharge at autopsy. Kistner [12] isolated the same organism from the nasal discharge of a person with a primary nasal tuberculoma. Schroeder [13] found diphtheria bacilli in 39 of 126 cases of chronic atrophic rhinitis and, in a few of these, B. mucosus. The diphtheria bacilli were identified by culturing the nasal secretion on Löffler's medium and appropriate Gram staining of the growth. Reference has already been made to our finding diphtheria bacilli in 1 of 2 cases of atrophic rhinitis. Jelin [14] found B. mucosus frequently in cases of atrophic rhinitis but concluded that this organism was not necessarily associated with the rhinitis. On the contrary, Elbert and Guerkess [15] concluded that B. mucosus was significant and its presence a relatively constant finding in association with atrophic rhinitis and rhinoscleroma. Mackey [16] reported a study of 85 children suffering from chronic nasal catarrh in whose nasal secretion he frequently found Pfeiffer's bacillus, Bacillus pertussis and B. mucosus. Miller [17] reported finding gonococci in the nasal secretion of a child with nasal infection and gonorrheal vaginitis. The organisms were identified by finding gram negative intracellular diplococci in the nasal secretion and differentiating them from the meningococcus by appropriate culture methods. Bordet [18] and Moncrieff and Lightwood [19] found B. pertussis in the nasal secretion of children with clinically diagnosed whooping cough. Hollender [20] and Shulman [21] isolated Vincent's fusiform bacilli and spirochetes in 2 cases of nasal infection. Fishbein and Staff,[22] studying a series of nasal infections, concluded that although staphylococci predominated in the largest number of cultures, the patients with streptococcic infections were the ones showing the most clinical symptoms, such as nasal discharge, obstruction to breathing, headache and lassitude. Tilley [23] studied the bacteriology of purulent nasal discharge and found that the flora was generally mixed but that staphylococci, streptococci and pneumococci were in evidence.

Bacteriology of the Sinuses.—Several observers, Toerne,[24] Linton,[25] Lewis and Turner [26] and Frankel,[27] studying clinically normal sinuses at autopsy, agreed that the sinuses are sterile in health. Frankel found that the pneumococcus was the predominant organism in sinuses which showed gross pathologic change. Oaks, Merrill and Oaks [28] studied the bacteriology of antral washings and found one or both of the maxillary sinuses sterile in 234 of 475 patients who came to treatment because of what they presumed to be sinus infection. No mention is made of the different types of organisms found, nor were roentgen studies made, but Oaks and his associates concluded that there are bacteria characteristic of sinusitis. Jenssen [29] concluded that normal sinuses are sterile but that there are

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no bacteria characteristic of sinusitis. Lederer and Livingston [30] and Collet [31] found the tubercle bacillus in 2 cases of maxillary sinusitis. Jay [32] described a case of maxillary sinus infection in which fusiform bacilli and spirilla were isolated. Ersner [33] made cultures in cases of maxillary sinusitis requiring operation and found that hemolytic and green-forming streptococci predominated but were most often found in association with nonsuppurative conditions. Lewis and Turner [34] made cultures of material from the antrum in 100 cases of suppurative maxillary sinusitis and isolated Pfeiffer's bacillus in 4, but streptococci, pneumococci and staphylococci predominated. Crowe and Thacher-Neville [35] studied 100 cases of paranasal sinus infection. Cultures of antral material taken at operation revealed streptococci (usually green-forming but occasionally hemolytic) to be the predominant organisms but Pfeiffer's bacillus and pneumococci were found occasionally. Babcock[36] concluded from culturing antral material that the pneumococcus is predominantly associated with acute sinusitis and green-forming streptococci with chronic sinusitis. Wirth [37] cultured material obtained from the antrums of 50 patients with purulent sinusitis. The predominating organisms encountered were Pfeiffer bacilli, hemolytic streptococci and pneumococci, staphylococci being seen but once. Kistner [38] studied nonsuppurative or "hyperplastic sinusitis," which he assumed to be a latent stage of sinus infection. Tissues removed from the antrums at operation were ground and washed in sterile sand and cultured. Material from more than 400 sinuses was thus cultured. A mixture of bacteria was usually present, but in 94.5 per cent streptococci were found, of which 35 per cent were hemolytic green-producing streptococci of type A, 14 per cent Streptococcus viridans and 18 per cent nonhemolytic streptococci of the gamma type. In addition to and in combination with the streptococci there were found, in order of frequency, staphylococci, M. catarrhalis, pneumococci, Friedlander's bacillus, the influenza bacillus, the colon bacillus, diphtheroid bacilli and streptothrices. Contrary to the observations cited, Ashley and Frich [39] found Staph. aureus more frequently than any other organism in a bacteriologic study of maxillary sinus infections in children.

SUMMARY AND CONCLUSIONS

Cultures of nasal secretion were made as a matter of routine for 500 patients admitted to a general medical service, none of whom had been admitted because of a primary complaint referable to the nose or the paranasal sinuses.

We find in agreement with most observers that the normal nasal flora consists chiefly of Staph. albus and diphtheroid bacilli, with Staph. aureus and M. catarrhalis less frequently.

Green-forming streptococci and pneumococci are occasional transients in the nasal cavity.

The presence of streptococci, pneumococci, B. mucosus, Pfeiffer bacilli and diphtheria bacilli indicates disease of the nasal mucosa or sinus disease or both.

The frequency with which green-forming streptococci, hemolytic streptococci and pneumococci were isolated by culture of nasal secretion in cases of sinusitis, acute or chronic, shows the diagnostic value of this simple, inexpensive procedure.

Frank Billings Medical Clinic.

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KAOLIN GRANULOMA OF THE STOMACH

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The harmful effects on the human body of silica and certain silicates have been known for many years. While references to the lesions in the lung are numerous and the changes caused by silicates in the muscle, peritoneum and serosa have been described, there have to our knowledge never been recorded the pathologic results of the silica group in the human stomach.

We present herewith a case of granuloma of the stomach which followed ingestion of medication containing colloidal kaolin (hydrated aluminum silicate, $Al_2Si_2O_8 + 5H_2O$) together with the results of preliminary experiments in rabbit stomachs using the same medicinal preparation.

PATHOLOGIC CONDITIONS CAUSED BY SILICA AND SILICATES

Silica and certain silicates cause characteristic reactions in tissue. This is a proliferative type of reaction in which there are nodules with mononuclear or giant cells enveloped by a fibrous tissue beyond which are scattered lymphocytes. There is great similarity of the reaction to that produced by the tubercle bacillus. Numerous authors have described this in detail.[1]

Gardner,[2] demonstrating the similarity of lesions produced by silica and the tubercle bacillus, showed that

From the Mount Zion Hospital.
Read before the Section on Gastro-Enterology and Proctology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

Dr. Franklin I. Harris, chief of surgery, gave permission to study this case. The pathologic investigations were made under the direction of Dr. G. Y. Rusk, chief pathologist to the Mount Zion Hospital. Mr. John Finn, consulting chemist for the State of California Compensation Insurance Fund and the Newmont Mining Company, collaborated in the mineralogical studies.

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the giant cells which develop in the tissues reacting to silica are not of the ordinary foreign body giant cell type. They resemble the Langhans cell of tuberculosis.

Silica (Si_2O), probably most active in colloidal form,[3] produces the typical lesion of silicosis, but certain of the silicates are also active dusts and produce a similar type of reaction. Notable among these are asbestos and talcum powder, magnesium silicate.[4]

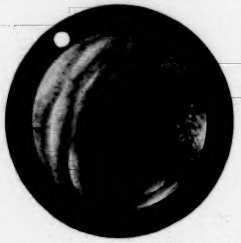

Fig. 1.—Gray nodule covered with numerous shiny excrescences revealed by gastroscopy on the posterior wall of the antrum.

Kettle[5] has produced lesions using kaolin. By analysis his specimens of kaolin were shown to contain particles of quartz and numerous fibers of sericite (potassium aluminum silicate), the majority measuring 3 microns or less. Jones, Carleton and Haynes also came to the conclusion that kaolin is a potentially dangerous dust. Whether it is the quartz or the sericite in kaolin which is responsible for the lesions has not been unequivocally determined.[6]

However, Kettle[5] points out, "with different forms of crystalline silica and with certain silicates essentially the same kind of lesion is produced, such modifications as occur depending on the size of the silica particles and their degree of solubility." Gardner[2] also agrees that the size of the particle is very important in the type and extensiveness of the lesion produced.

With this knowledge, namely that silica and certain silicates may produce a specific type of granulomatous reaction in various tissues of the body, we may now consider their effect on the gastric mucosa.

REPORT OF CASE

History.—A white man aged 37, an automobile mechanic, had abdominal pain, pyrosis, nausea and vomiting over a period of eight years. He had no permanent relief from various medications or diet. A diagnosis of duodenal ulcer had been previously made, but roentgenographic studies made subsequently were essentially negative. A later diagnosis of colitis had been made erroneously.

Physical examination revealed nothing of significance excepting epigastric tenderness.

The urine, stool, blood count, sedimentation rate and Wassermann reaction were normal. The gastric analysis revealed free hydrochloric acid 68-86 and total acid 77-102.

A gastroscopic examination was made with the 50 degree angle flexible gastroscope. The mucosa of the prepyloric region was thickened. A gray nodular area approximately 2 cm. in diameter was present on the posterior wall of the antrum immediately distal to the angulus (incisura). This nodule was rounded and irregular; the surface was covered with numerous shiny excrescences (fig. 1).

The rugae of the midportion of the body of the stomach were hypertrophied.

Roentgen examination two days later revealed a mild degree of hypertrophic gastritis and duodenitis. The lung fields were clear.

Despite the essentially negative findings, it was thought that the long history of symptoms and the unusual gastroscopic observations were indications for surgery. A subtotal gastrectomy was done five days later.

Gross examination of the stomach after its removal showed evidence of an old healed duodenal ulcer. No lesion as described gastroscopically was seen, much to our chagrin.

The patient became asymptomatic and has remained so for over two and one-half years.

During the early postoperative period we awaited with anxiety the histologic report.

Microscopic Study.—At the base of the mucosa were a few irregularly spaced lesions of a granulomatous nature. These were made up of nodules of a definite achitecture. The center of the nodule contained a large cell which was multinucleated, granular and usually fairly large. The nuclei of many of the giant cells tended to congregate about the periphery.

Encapsulating this cell was a delicate fibrous tissue which was not usually excessive in amount. Beyond the connective tissue might be seen plasma cells, lymphocytes and eosinophilic luekocytes. They were not present in sufficient numbers to constitute a real zone.

In a few of the giant cells there was foreign material (figs. 2 and 3). This varied in size and shape and was colorless and refractile. Some of the particles looked like laminated spicules. Occasionally, fragmented material took a blue stain with hemotoxylin.

Fig. 2.—Nodular areas near the base of the mucosa. In the central part of the nodules giant cells are present, some of which surround foreign material.

Fat, Masson, Kossa and acid-fast stains were negative.

Mineralogical Analysis.—A study was made of the crystals in the giant cells and in the residue of tissue after microincineration. They were insoluble in water, hydrochloric acid

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and nitric acid. The crystals varied in size from 2 to 4 microns and belong to the hexagonal system. They were anisotropic or doubly refractive. The Becker line showed them to have a higher refractive index than Canada balsam (1.54). They had the same general morphologic appearance as the crystals present in the colloidal kaolin examined and the crystals present in the preparation used by the patient. They had the characteristics of silica.

Fig. 3.—Type of giant cell typical in silicosis surrounding foreign material. The nuclei tend to congregate around the periphery. The material is fragmented, laminated, colorless and refractile. Some of it stains blue with hematoxylin.

Preliminary Experiments on Rabbits.—With the medicament which the patient had been taking, a test experiment on rabbit stomach was undertaken. The preparation consisted of English kaolin colloidal 20 per cent and aluminum hydroxide 2.5 per cent in liquid petrolatum. We report here the findings of this "scout" experiment.

Two series of animals were tested. In the first series 2 cc. of the medication was injected into the gastric mucosa of 3 rabbits.

In series 2 a small area of the stomach mucosa of 4 rabbits was lightly curetted and the animals were fed daily a diet into which was incorporated powdered colloidal kaolin.

The rabbits of series 1 were killed at one, one and one-half and four months respectively after injection. Gross mucosal elevations or nodules were present. The microscopic examination showed groups of giant cells at the periphery of the injected material.

All the giant cells had multiple nuclei, many of which tended to group themselves peripherally or at the end of the cell like those of a Langhans cell. Colorless refractile crystals were present in many of the giant cells (fig. 4).

In the scarified series the same type of reaction was found; in fact there was greater similarity to the human case in these animals. No gross mucosal lesions were found in these animals. However, there were microscopic changes in the submucosa. Multinucleated giant cells occurred singly or in groups and were encapsulated by a fine loose connective tissue, surrounded by lymphocytes, plasma cells and eosinophilic neutrophils. Some of the giant cells contained foreign material. The most striking particles were sharp pointed clear refractile spicules.

There were giant cells about the suture material, but they were of the true foreign body type, which has little resemblance to the specific kind observed in silicosis.

The foreign material had the colorless glassy refractile appearance which characterized some of the particles of the kaolin which was examined in water suspension under the microscope for comparison.

COMMENT

Evidence has been presented to permit the reasonable conclusion that kaolin may cause a granulomatous inflammatory reaction in the stomach. This reaction is similar to that which is typical of the silica group.

Many unknown factors prevent any additional conclusions. We should like to know the conditions necessary for the silicates to produce this inflammatory reaction in the stomach. We should like to know how common this disease is. If the known reaction to silica and to silicates was accidentally discovered in this 1 case, might it not be reasonable to presume that there may be other undiagnosed cases?

We might perhaps be warranted in suggesting that patients using similar preparations be carefully observed and with the gastroscope. If symptoms should occur suggesting gastrointestinal irritation or if no relief should be obtained from the original symptoms, the possible deleterious effects of this group should be considered.

This case also illustrates the value of gastroscopy followed by tissue studies.

SUMMARY

A histopathologic and mineralogical investigation was made of the stomach of a patient who had been ingesting a preparation containing kaolin for a long period of time. Clinical and roentgen examinations revealed no gastric disease. Gastroscopy showed a prepyloric tumor, which however was not seen in the gross resected stomach. Microscopic studies proved the lesion to be a granuloma, with the type of foreign body giant cell present in the lesions of silicosis. Mineralogical studies confirmed the presence of silica in the gastric tissues.

In experimental studies on rabbits it was possible to reproduce the lesions typical of silica irritation which were similar to those found in the human case.

Fig. 4.—Type of giant cell in the rabbit stomach into which the kaolin containing medication of the patient was injected is large with numerous nuclei at the periphery of the cells. Several colorless refractile crystals are seen.

450 Sutter Street.

CLINICAL INDICATIONS FOR INDUCING GASTRIC HYPOMOTILITY

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The motor activity of the human stomach is of demonstrable clinical significance. This is particularly true in those patients with lesions involving viscera innervated by the extended vagi. Moreover, it appears that the clinical management of certain patients may often be aided by an increased knowledge of stomach activity.

Members of the Surgical Research Department of the Ohio State University have during the past few years investigated the motor activity of the stomach of a large number of patients under a variety of clinical conditions. Using the balloon and kymograph method, we have found that the normal motility is affected not only by disturbances in gastric physiology but also by certain pathologic lesions occurring elsewhere along the gastrointestinal tract.

More recently we have studied alterations in the motor activity which may be observed in patients presenting certain common abdominal complications. Many patients complained of pain or discomfort simultaneously with obvious kymographic evidence of gastric hypermotility. Conversely, the patients ceased to complain of pain or distress when the stomach was demonstrably quiescent, whether that quiescence was spontaneous or induced by the administration of certain drugs. It is our purpose in this paper to present briefly the background of the present studies and then to draw attention to the clinical indications for inducing hypomotility of the human stomach.

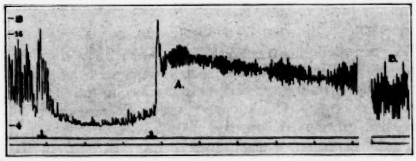

Fig. 1.—Effect of atropine (given at 1) on the motility of the normal human stomach and the reversal of this effect by morphine (given at 2). Note the lowered tonus and decreased gastric activity following administration of atropine. Courtesy of Journal of Pharmacology and Experimental Therapeutics.[3]

In an investigation of the influence of the extrinsic innervation on the motor activity of the human stomach [1] it was concluded that the vagus and splanchnic nerves carry both motor and inhibitory fibers. The effect on the stomach of stimulation of either nerve depends to a certain degree on the existing gastric tonus, although the vagus is chiefly motor while the splanchnic has chiefly an inhibitory effect. Bilateral splanchnic resection was followed by increased gastric activity, which persisted. Left subdiaphragmatic vagotomy was followed by decreased gastric activity, which persisted.

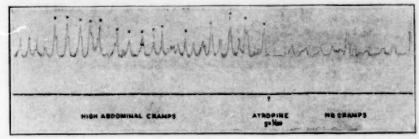

Fig. 2 (B. K., Dec. 7, 1938).—The control of postoperative "gas pains" four days after splenectomy. Severe pains were noted at the peak of the indicated contractions. Coincident with the onset of gastric hypomotility there was complete relief.

Following laparotomy the normal human stomach remains quiescent for from twenty-four to seventy-two hours.[2] This is followed by gastric hypermotility accompanied by abdominal distress, which is usually interpreted by the patient as "gas pains." The gastric hypermotility persists for about fourteen days postoperatively, but during the latter part of the period the patients often interpret the increased activity as hunger.

The effects of the administration of atropine, morphine and prostigmine were also determined.[3] Morphine was predominantly motor. Atropine was constantly inhibitory. Morphine and atropine were mutually antagonistic, either drug counteracting the effect of the other (fig. 1). Prostigmine in the majority of instances inhibited the activity of the human stomach. Moreover, administration of prostigmine or atropine after the previous administration of either drug was uniformly followed by gastric hypermotility.[4]

With these studies as a background we are now investigating the motor activity of the human stomach during the course of common abdominal complications. We have continued to use the balloon and kymograph method.[5] The motility graphs have been analyzed according to the MacQuigg classification.[6]

TABLE 1.—*Analysis of Gastric Motility During Control of the Postoperative Syndrome of "Gas Pains" (B. K.)*

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
"Gas pains" 4 days postoperative 12/7/38	1. Observation	5	23	32.5	26	8 of 40 to 53 mm.	1	Severe epigastric cramps indistinguishable from "gas pains" noted with indicated contractions
	2. Atropine 1/120 grain intravenously	3	13	15.5	11	2 of 36 mm.	1½	No clinical discomfort during this period of decreased gastric activity

From the Department of Research Surgery, Ohio State University.

This investigation was aided by a grant from the Development Fund of the Ohio State University.

The Abbott Laboratories, Inc., supplied the intravenous preparations of atropine used in this investigation.

Read before the Section on Gastroenterology and Proctology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

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CONTROL OF POSTOPERATIVE ABDOMINAL CRAMPS INTERPRETED AS "GAS PAINS"

Barron, Curtis and Lauer [2] observed a consistent period of gastric hypermotility following laparotomy. During the early part of the hyperactive period the patients often complained of "gas pains," although in most instances there was no evidence of abdominal distention. We have investigated the gastric motility in such a patient four days following splenectomy. During the period of observation the patient complained of high abdominal cramps, clinically similar to "gas pains." There was no abdominal distention, the wound was clean and there were no demonstrable postoperative complications.

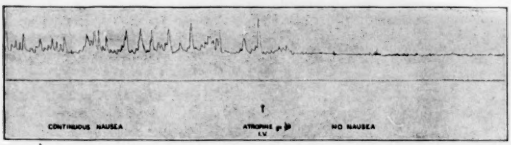

Fig. 3 (K. H., Nov. 10, 1938; esophagopleural fistula; nausea six days following apical thoracoplasty; balloon introduced into stomach through gastrostomy stoma).—Control of late postoperative nausea. Continuous nausea was observed throughout the period of gastric hyperactivity. Coincident with the onset of gastric hypomotility there was complete relief.

The kymograph records reveal continuous high type 5 contractions. At the apex of each of the higher contractions the patient complained of a severe upper abdominal cramp, clinically indistinguishable from a "gas pain" (fig. 2). Moreover, the intensity of the pain appeared to vary with the amplitude of the recorded contraction.

Immediate partial inhibition of gastric motility was observed following the intravenous administration of $\frac{1}{150}$ grain (0.4 mg.) of atropine. Coincidentally with the decreased gastric activity, the patient was completely relieved of the abdominal cramps and did not again complain of pain or distress during the entire period of reduced activity (table 1, fig. 2).

On this and at subsequent observations symptomatic relief of postoperative abdominal cramps interpreted as "gas pains" was effective as long as the stomach remained quiescent. This period, usually two to three hours in length, was the usual duration of the drug effect.

CONTROL OF LATE POSTOPERATIVE NAUSEA

Postoperative nausea may be immediate or late. Immediate postoperative nausea is frequently observed as the patient recovers from the effects of a general or even of a local anesthetic. It is usually a self-limited condition. Late or prolonged postoperative nausea, however, may be a serious complication and at times indicates a grave physiologic disturbance. The etiology of late postoperative nausea may be so diversified that no single mechanism may be responsible. It appears, however, that unusual gastric activities often described clinically as "reverse peristalsis" are a common finding in this condition.

Gastric activity during the course of late postoperative nausea was studied on a patient on whom a gastrostomy had previously been accomplished. Following a second operation the patient remained nauseated for six days. The balloon was introduced directly into the stomach through the gastrostomy stoma with no inconvenience to the patient. The kymograph recorded continuous irregular activity of the stomach consisting largely of type 6 motility (fig. 3). During the entire observation period the patient complained of continuous nausea.

Administration of $\frac{1}{150}$ grain of atropine intravenously was quickly followed by a diminution of gastric activity. Simultaneously with the decreased gastric activity the patient was completely relieved of the sensation of nausea and did not again complain of nausea as long as the stomach was inactive (table 2, fig. 3).

EFFECT OF DUODENAL ULCER WITH OBSTRUCTION ON GASTRIC MOTILITY

A duodenal ulcer may frequently alter the emptying time of the stomach. This is particularly true of obstructive ulcers. However, there has been but little investigation of the relation of the clinical symptoms to abnormal gastric activity in the ulcer patient.

TABLE 2.—*Analysis of Gastric Motility During Control of Late Postoperative Nausea (K. H.)*

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
Nausea 6 days postoperative 11/10/38	1. Observation	6 & 8	33	17	50	2 of 41 to 48 mm.	2	Continuous nausea
	2. Atropine $\frac{1}{150}$ grain intravenously	1 & Q	24	6	5	2 of 10 mm.	20	Complete cessation of nausea

N. U., a white man aged 47, was admitted to the University Hospital with a partial pyloric obstruction due to a benign ulcer of the first part of the duodenum. The patient had been under medical care for the preceding twelve years. Obstructive symptoms had been present for two months before he entered the hospital. Several preoperative gastric motility investigations were accomplished. During these observations it became possible to control the symptoms of "pylorospasm." [7] Posterior gastrojejunostomy was then accomplished. A number of postoperative observations have been made.

During one of the preoperative motility studies the balloon was swallowed and the recording started while the patient was complaining of severe cramping epigastric pain that clinically was indistinguishable from the usual symptoms of "pylorospasm." At this time there was obvious kymographic evidence of greatly increased gastric motility, largely type 5 and 8 contractions (table 3, fig. 4).

Following the administration of $\frac{1}{150}$ grain of atropine intravenously, the stomach quickly became hypomotile with an ensuing immediate relief from the distress. Moreover, the patient did not again complain of epigastric pain as long as the stomach was demonstrably quiescent.

At the beginning of another preoperative observation the patient had no pain and was quite comfortable, and the kymograph showed but little gastric activity. Soon spontaneous gastric hypermotility became evident, and coincidentally with the greatly increased type 5 activity the patient complained

7. Hamilton, F. E., and Curtis, G. M.: The Effect of Duodenal Ulcer with Obstruction on the Motor Activity of the Human Stomach, Rev. Gastroenterol., to be published.

of severe cramping pain, clinically indistinguishable from that of "pylorospasm" (table 3, fig. 5).

This period of epigastric pain associated with gastric hypermotility was of short duration and was terminated by a spontaneous remission of the increased gastric activity. Again, cessation of pain occurred simultaneously with the onset of cystic duct and common duct. Preoperatively the patient had occasional attacks of upper abdominal pain clinically indistinguishable from biliary colic.

During such an attack the motility of the stomach was investigated.[8] The balloon was passed without

TABLE 3.—*Analysis of Gastric Motility During Control of "Pylorospasm" Due to Obstructive Duodenal Ulcer (N. U.)*

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
"Pylorospasm" preoperative 2/1/39	1. Observation	5 & 8	21	33.5	34	2 of 68 to 81 mm.	1½	Continuous severe epigastric cramps indistinguishable from "pylorospasm"
	2. Atropine 1/150 grain intravenously	Q	33	..	..	.....	...	Complete cessation of pain
"Pylorospasm" preoperative 2/2/39	1. Observation	Q	10	..	..	.....	...	No subjective pain
		5	10	30	6	1 of 39 mm.	1½	Spontaneous gastric activity
		6M	2	29	7	1 of 56 mm.	0	Severe epigastric cramps indistinguishable from "pylorospasm"
		5M	12	66	13	1 of 116 mm.	1	
		Q	23	..	..	.....	...	Spontaneous gastric quiescence; no subjective pain
		1	23	20	7	1 of 48 mm.	5	

gastric hypomotility and persisted as long as the stomach remained quiescent.

It was found at operation that the patient had a benign, obstructive, duodenal ulcer with a partial pyloric stenosis. Under these conditions intermittent "pylorospasm" is a common clinical finding. It is consequently possible and even probable that the intermittent preoperative epigastric distress experienced by the patient was actually due to "pylorospasm." It cannot be concluded that the preoperative periods of spasmodic gastric hypermotility were kymographic evidences of "pylorospasm."

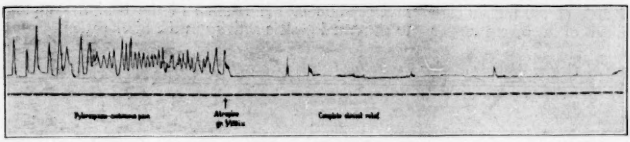

Fig. 4 (N. U., Feb. 1, 1939).—Symptomatic control of "pylorospasm" due to benign obstructive duodenal ulcer. Continuous epigastric pain indistinguishable from that of pylorospasm was noted throughout the initial period of gastric hyperactivity. Complete clinical relief was noted coincident with gastric hypomotility induced by the intravenous administration of atropine.

difficulty, and continuous type 6 activity was observed (table 4, fig. 6). This irregular type of gastric hypermotility was unchanged throughout an observation period of forty minutes, while during the entire period the patient complained of upper abdominal pain indistinguishable from that of biliary colic. Following administration of 1/150 grain of atropine intravenously there was complete cessation of gastric activity and simultaneous cessation of pain. As in the previous investigation, the patient remained comfortable as long as the stomach was quiescent.

Biliary colic is thought to stimulate reflexly the stomach by means of the extended vagus (Barber and Stewart,[9] McCrea [10]), Several investigators, Held and Roemer,[11] Smith and Miller [12] and others, have shown

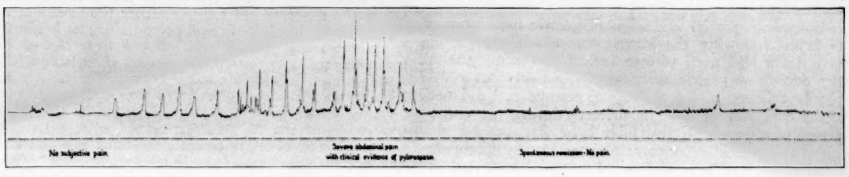

Fig. 5 (N. U., Feb. 2, 1939).—Symptomatic control of "pylorospasm" due to benign obstructive duodenal ulcer. At the beginning the patient felt no pain. Coincident with spontaneous gastric hyperactivity the patient complained of pain indistinguishable from that of pylorospasm. This period was terminated by a spontaneous remission of gastric activity, and throughout the hypomotile period the patient felt no pain.

Since the tube length is kept constant during a given series of gastric motility studies, x-ray studies reveal that the balloon records the activity of the body of the stomach.[5] It would consequently appear that in this investigation hypermotility of the body of the stomach occurred simultaneously with clinical evidence of "pylorospasm"; moreover, that the patient was free from pain when the stomach was demonstrably quiescent.

EFFECT OF BILIARY COLIC ON GASTRIC MOTILITY

The relation of gastric motility to biliary colic was studied on a patient who at subsequent operation was shown to have cholelithiasis involving the gallbladder, that disease of the gallbladder, and in particular cholecystitis with cholelithiasis, stimulates gastric activity. The subjective pain in this instance may not have been

8. Hamilton, F. E.: The Clinical Significance of Human Gastric Motility, Ann. Surg. **114**: 153 (July) 1941. Barron, Curtis and Lauer.[2]
9. Barber, W. H., and Stewart, G. D.: Further Observations on Reflex Gastric Hypermotility, Proc. Soc. Exper. Biol. & Med. **17**: 155, 1919-1920.
10. McCrea, E. D'A.: The Nerves of the Stomach and Their Relation to Surgery, Brit. J. Surg. **13**: 621 (April) 1926.
11. Held, I. W., and Roemer, J.: Gastrospasm: A Clinical and Roentgenological Study, Am. J. M. Sc. **164**: 188 (Aug.) 1922.
12. Smith, F. M., and Miller, G. H.: A Study of the Reflex Influence of the Colon, Appendix and Gallbladder on the Stomach, Am. J. Physiol. **90**: 518, 1929.

due to gastric hypermotility; nevertheless, the motility of the stomach might be an index of the relative activity of another organ having a similar nerve supply.

CONTROL OF CONTINUOUS NAUSEA AND REGURGITATION ASSOCIATED WITH PARTIAL OBSTRUCTION OF THE STOMACH DUE TO AN ADVANCED CARCINOMA

W. C., a white man aged 70, was admitted to University Hospital complaining of continuous nausea and regurgitation, inability to retain solids or liquids, loss of weight and general debility. A carcinoma which involved practically the entire stomach was later demonstrated at operation. The esophagus and the fundus were not involved in the malignant process.

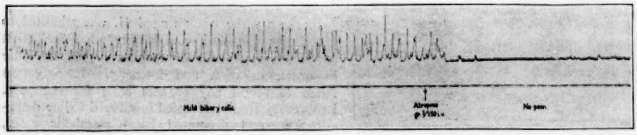

Fig. 6 (N. K., Feb. 6, 1939).—Symptomatic control of biliary colic due to cholecystitis with cholelithiasis. Continuous upper right quadrant pain indistinguishable from that of biliary colic was noted throughout the entire period of gastric hypermotility. Complete clinical relief was noted coincident with gastric hypomotility induced by the intravenous administration of atropine.

It was found necessary to administer 1/100 grain (0.6 mg.) of atropine intramuscularly before the patient could swallow the balloon to begin the motility investigation. Thirty minutes later he swallowed the balloon easily, and the kymograph then revealed tremendously increased gastric activity, type 8 associated with continuous nausea and regurgitation (table 5, fig. 7).

An intravenous injection of 1/150 grain (0.4 mg.) of atropine was followed by little change in the hyperactivity of the stomach or in the clinical symptoms. Again 1/150 grain of atropine was administered intravenously and was followed by decreased gastric activity associated with considerable clinical relief.

It should be noted that no results were observed until a total of 1/43 grain (1.5 mg.) of atropine had been administered within a relatively short period of time. Finally the cumulative effect of this large amount of atropine was followed by greatly decreased type 1 motility, and for as long as the hypomotility continued the patient was quite comfortable. When the hyperactivity of the stomach was controlled by the adminis-

TABLE 4.—*Analysis of Gastric Motility During Control of Biliary Colic (N. K.)*

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
Biliary colic preoperative 2/6/39	1. Observation	6M	38	40	72	5 of 58 to 68 mm.	½	Continuous upper right abdominal cramps indistinguishable from biliary colic
	2. Atropine 1/150 grain intravenously	Q	19	..	..	.....	...	No subjective pain

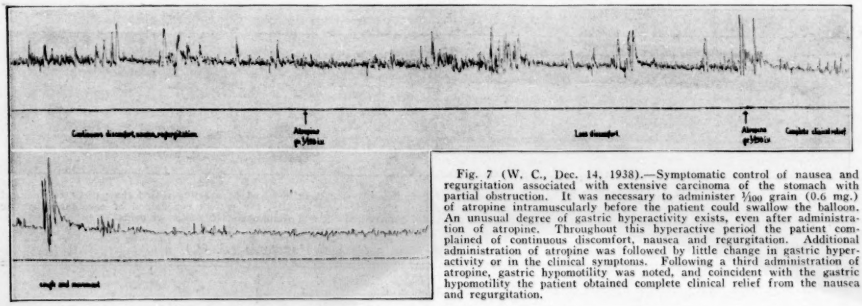

Fig. 7 (W. C., Dec. 14, 1938).—Symptomatic control of nausea and regurgitation associated with extensive carcinoma of the stomach with partial obstruction. It was necessary to administer 1/100 grain (0.6 mg.) of atropine intramuscularly before the patient could swallow the balloon. An unusual degree of gastric hyperactivity exists, even after administration of atropine. Throughout this hyperactive period the patient complained of continuous discomfort, nausea and regurgitation. Additional administration of atropine was followed by little change in gastric hyperactivity or in the clinical symptoms. Following a third administration of atropine, gastric hypomotility was noted, and coincident with the gastric hypomotility the patient obtained complete clinical relief from the nausea and regurgitation.

TABLE 5.—*Analysis of Gastric Motility During Control of Continuous Nausea and Regurgitation Associated with Carcinoma of the Cardia with Stenosis (W. C.)*

Case	Investigation	Type	Length, Mm.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
Carcinoma of cardia 12/14/38	1. Observation	8	37	13	427	8 of 51 to 56 mm.	0	Continuous nausea and regurgitation; atropine 1/100 grain administered intramuscularly 30 minutes before start of record
	2. Atropine 1/150 grain intravenously	8	36	12	330	5 of 53 to 80 mm.	0	Less subjective discomfort
	3. Atropine 1/150 grain intravenously	1	44	11.3	77	1 of 66 mm.	0	Complete clinical relief

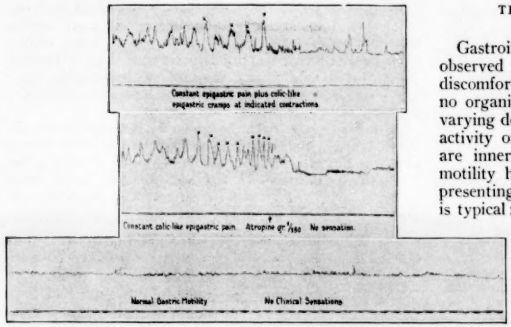
Constant epigastric pain plus colic-like epigastric cramps at indicated contractions
Constant colic-like epigastric pain
Atropine gr 1/150
No sensation
Normal Gastric Motility
No Clinical Sensations

Fig. 8 (B. H.).—Control of the abdominal discomfort observed in certain patients with hypothyroidism. During the period of gastric hyperactivity the patient complained of epigastric pain, with severe cramps at the apex of the indicated contractions. When the stomach was quiescent the patient felt no pain. This was true whether the gastric quiescence was spontaneous, as in the first graph (June 20, 1939), occurred following administration of atropine, as in the second graph (June 21) or was observed following adequate thyroid and iodine therapy for the control of hypothyroidism, as demonstrated in the third graph (August 2). (Courtesy of the Journal of Clinical Endocrinology.[13])

THE RELATION OF GASTRIC MOTILITY TO HYPOTHYROIDISM

Gastrointestinal symptoms may occasionally be observed in certain patients with hypothyroidism. The discomfort usually consists of abdominal pain for which no organic basis can be demonstrated. The pain is of varying degree and appears to be associated with hyperactivity of portions of the gastrointestinal tract which are innervated by the extended vagus. The gastric motility has been determined in several such patients presenting proved hypothyroidism. The following case is typical:[13]

B. H., a white woman aged 41, was admitted to University Hospital complaining of constipation and frequent attacks of epigastric pain, variable in onset, duration and intensity. Investigation failed to reveal any organic basis for the pain. Laboratory studies revealed low blood iodine determinations and decreased basal metabolic rates, which along with the clinical findings was interpreted as evidence of hypothyroidism.

A motility investigation revealed irregular gastric hyperactivity, type 5, associated with constant epigastric pain plus colic-like epigastric cramps at the indicated contractions (table 6, fig. 8). On the following day the kymograph recorded constant irregular hyperactivity associated with colic-like epigastric pain. Following administration of adequate amounts of atropine, the patient was able to swallow and retain liquids.

By this means the patient was kept fairly comfortable throughout the duration of his period of hospitalization.

TABLE 6.—*Analysis of Gastric Motility in a Case of Hypothyroidism (B. H.)*

(Complaints: Constipation, Epigastric Pain. Basal Metabolic Rate −12. Blood Iodine 2.7 Micrograms per Hundred Cubic Centimeters)

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
Hypothyroidism 6/20/39	1. Observation	5	24.4	43	26	Maximum of 24	2.8	Dull epigastric pain, with cramps at 4 peaks
6/21/39	1. Observation	5	7.3	64	7	Maximum of 37	0.7	Colic like epigastric pain
		6	7.2	59	12	9 of 25-43	0	
	2. Atropine sulfate 1/150 grain intravenously	Q	8.3	51	..	.....	..	Relief of pain
	(After Treatment of Hypothyroidism; No Complaints. B. M. R. +1)							
8/2/39	1. Observation	2	45.0	46	?	Maximum of 13	0	Normal gastric motility; no clinical sensations

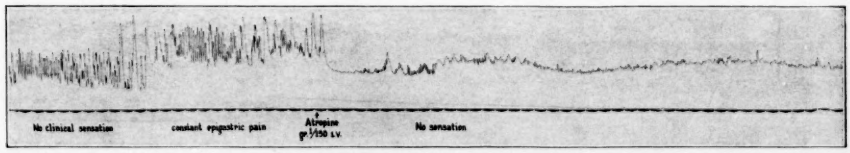

Fig. 9 (F. H., April 8, 1939).—Control of the symptom complex of "vagotonia." During the initial hyperactive period the patient experienced no pain. However, following a spontaneous rise in tonus, with no change in the gastric hyperactivity, the patient complained of constant epigastric pain. Administration of atropine was followed by a lowered tonus, decreased gastric activity and simultaneous cessation of pain.

TABLE 7.—*Analysis of Gastric Motility in a Case of Vagotonia (F. H.)*

Case	Investigation	Type	Length, Min.	Average, Mm.	Number of Contractions	Number of Contractions of Maximum Amplitude, Range Mm.	Maximum Intervals, Min.	Comment
Vagotonia 4/8/39	1. Observation	8	10.5	34	58	1 of 93	0	No clinical sensations
		7	14	60	59	4 of 57-63	¼	Constant epigastric pain
	2. Atropine sulfate 1/100 grain intravenously	Q	2	47	..	.....	...	Complete relief of pain
		4	6.5	43	31	1 of 29	0	
		3	9	56	41	3 of 12-15	0	No sensations
		2	30	50	130	4 of 10-15	0	

13. Hamilton, F. E.; MacQuigg, R. E., and Curtis, G. M.: The Gastric Motility in Certain Patients with Thyroid Deficiency, J. Clin. Endocrinol. **1**: 24 (Jan.) 1941.

tration of 1/150 grain of atropine intravenously there was immediate cessation of gastric hypermotility with simultaneous cessation of the epigastric pain. The patient was then treated for hypothyroidism by the administration of desiccated thyroid and iodine.

Six weeks later, following a satisfactory clinical response to this treatment, investigation revealed a normal basal metabolism plus normal gastric motility. Moreover, the patient had ceased to complain of abdominal pain (table 6, fig. 8).

RELATION OF GASTRIC MOTILITY TO THE SYMPTOM COMPLEX KNOWN AS "VAGOTONIA"

Rather frequently patients are seen who are classed clinically as neurotic. In certain of these persons investigation will reveal that the discomfort of which they complain appears to be limited to the distribution of the extended vagus. In some of these no organic basis can be demonstrated to account for the pain. To this delimited group of patients the term "vagotonia" has been applied.[14] Admittedly the term "vagotonia" is, indeed, inclusive, yet clinically it appears to apply well in this symptom complex. The alterations in gastric motility have been investigated in a number of such patients, as is exemplified in the following case:

F. H., a white housewife aged 46, was admitted to University Hospital complaining of dull, more or less constant epigastric pain. Thorough investigation failed to reveal an organic basis for the pain. There was no evidence of hypothyroidism. At the beginning of a motility study the patient stated that she was quite comfortable and had no pain. However, the kymograph recorded greatly increased gastric activity, type 7. After an interval a spontaneous elevation of tonus was observed, associated with the same type of gastric activity, and at once the patient complained of constant epigastric pain. Administration of atropine was followed by a lowered tonus, decreased gastric activity and simultaneous cessation of pain (table 7, fig. 9). Throughout the investigation the patient did not complain of epigastric discomfort when the stomach was quiescent.

CONCLUSIONS

By the balloon and kymograph method hypermotility of the human stomach has been demonstrated during the clinical appearance of "gas pains," late postoperative nausea, "pylorospasm" due to obstructive duodenal ulcer, biliary colic, the nausea and regurgitation associated with advanced carcinoma of the stomach, certain instances of hypothyroidism and "vagotonia."

In all gastric hypermotility occurred simultaneously with the varying degrees of clinical distress or discomfort. Moreover, the patients ceased to complain of pain or discomfort when the stomach was quiescent. Whether the gastric hypomotility was spontaneous or induced by the administration of atropine made no apparent difference. At the onset of hypomotility the patients ceased to complain of distress.

From these clinical studies it appears that the motility of the human stomach may be regarded as an indicator of certain types of abnormal activity of the gastrointestinal tract. Control of the gastric hypermotility in such instances will often simultaneously control the clinical symptoms associated with the primary condition.

14. Eppinger, Hans, and Hess, Leo: Vagotonia, Nervous and Mental Disease Monograph 20, New York, Nervous & Mental Disease Publishing Company, 1917.

The Electron Microscope.—It is believed that in the newly invented electron microscope using electronic waves 1/100,000th of the wavelength of visible light, 25,000 to 100,000 magnification with accompanying resolution can be attained.—Gage, Simon H.: The Microscope, Ithaca, N. Y., Comstock Publishing Company, Inc., 1941.

CHRONIC ALCOHOLIC GASTRITIS

EVALUATION OF THE CONCEPT, WITH GASTROSCOPIC STUDIES IN ONE HUNDRED CASES

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CHICAGO

Widespread drinking of alcoholic beverages goes back at least to the epicures of antiquity. Laymen and physicians alike have conjured up in their minds a frightful picture of the ravages of alcohol on the lining of the human stomach. Thirty or forty years ago gastritis, and especially alcoholic gastritis, was widely diagnosed on the basis of the character of the secretions removed by the stomach tube. The presence of a large amount of mucus was the essential factor in the diagnosis of "gastric catarrh," or chronic gastritis. In later years gastritis was regarded as a loose term which included many digestive symptoms. Chronic inflammation of the stomach as a definite organic entity was regarded as rare. For a long time it was taught, and in some centers it is still taught, that the one excellent example of chronic gastritis is that due to the chronic use of alcoholic beverages.

Within the last few years, with the aid of the flexible gastroscope, chronic gastritis has been shown to be widespread and to be an important organic entity in persons who do not use alcoholic beverages at all. The statistics of Schindler [1] on a group of 1,000 persons with dyspepsia in America and on a smaller group in Germany showed 41 and 45 per cent, respectively, with chronic gastritis. My recent statistics [2] based on 800 gastroscopic examinations showed 43.3 per cent of persons with dyspepsia in the gastrointestinal clinic of the Provident Hospital to have chronic gastritis. In none of the groups mentioned was there a significant number of chronic alcoholic addicts. It has become evident to all gastroscopists that certainly persons other than alcoholic addicts may have chronic gastritis. The question therefore arises What really is the role of alcohol in chronic gastritis, in the light of the more recent advances in this field?

In order to reevaluate the clinical concept chronic alcoholic gastritis, I first reviewed the literature for convincing evidence of experimental alcoholic gastritis in animals and postmortem evidence of the disease in man. Secondly, I undertook to select a fairly large group of persons who unquestionably were alcoholic addicts, to examine them gastroscopically and to correlate certain clinical data with the gastroscopic picture.

EXPERIMENTAL ALCOHOLIC GASTRITIS

Friedenwald [3] in 1905 fed 50 per cent alcohol to a large group of rabbits for several weeks and found that he could not consistently produce gastritis. Fahr [4] in 1911 attempted to produce irritation gastritis in 5 rabbits. He found mild hyperemia, but the gastric tissue was microscopically normal. One of the most

From the Division of Gastroenterology, Provident Hospital.
The chemical studies were made by Clover Oliver, Harriet Thompson and Mary Hamilton.
The chest fluoroscopy was done by Drs. Robert G. Bloch, William B. Tucker and J. E. Bryant.
Read before the Section on Gastro-Enterology and Proctology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Schindler, Rudolf: Incidence of Various Types of Gastric Disease as Revealed by Gastroscopic Studies, Am. J. M. Sc. **197**: 509 (April) 1939.
2. Berry, L. H.: Etiological Relationships of Chronic Gastritis: A Preliminary Report, Proc. Inst. Med. Chicago **13**: 14 (May 15) 1941.
3. Friedenwald, Julius: The Pathologic Effects of Alcohol on Rabbits, J. A. M. A. **45**: 780 (Sept. 9) 1905.
4. Fahr: Beitrage zur Frage des chronischen Alkoholismus, Virchows Arch. f. path. Anat. **205**: 397, 1911.

interesting animal experiments was that of Thomsen,[5] who in 1925 introduced 50 per cent and 95 per cent alcohol into the Pavlov pouch of a dog at intervals over a period of eight months. He reported that after one month the dog's stomach showed hypersecretion, with

TABLE 1.—*Anamnesic and Laboratory Data on Alcoholic Addicts*

Age: 80% in 3d, 4th or 5th decade	
Sex: 97% male, 3% female	
Race: 75% white, 24% Negro, 1% Mexican	
Habits	
Days intoxicated	
Average among 40 subjects, 3 to 6 days	
Days sober	
Average, 4 or 5 days	
Years of drinking	
1 to 55; 75% of 74 subjects had been drinking 15 years or more	
Beverage	
Straight whisky; wine (20% alcohol); beer; denatured alcohol; home-brew; miscellaneous alcoholic beverages	
Amount consumed daily	
40 subjects: average, 2 to 3 pints whisky; 8 subjects: average, 3.3 pints of wine	
Use of tobacco	
33 subjects: average, 21 cigarets per day; 90% smokers	
Symptoms	
Delirium tremens	
47 of 57 subjects had delirium tremens at some time	
Cramps in limbs	
33 of 52 subjects affected (very little frank polyneuritis)	
Hallucinations	
25 of 50 subjects affected	
Laboratory data	
Wassermann and Kahn reactions	
7% positive, 93% negative	
Fluoroscopy of chest	
7 of 88 subjects, tuberculous lesions	
Hemoglobin content (Sahli)	
25 of 61 subjects, 75% or less	
Blood vitamin C level	
49 of 55 subjects, below normal (0.7 mg.)	
Fractional histamine tests	
7 of 56 showed achlorhydria	

a great increase in mucus. A biopsy and histologic sections showed acute inflammation. During a two month rest period the mucosa returned to normal, grossly and microscopically. Eight months after the termination of the alcohol feeding the animal became progressively more debilitated and died. Autopsy showed extensive atrophic gastritis. While Thomsen was inclined to interpret the profound atrophy as due to the chronic effect of alcohol, I feel that any chronic debility is likely to be associated with atrophic changes in any organ and that one could not justifiably conclude that the atrophy in the dog's stomach was the direct effect of alcohol.

PATHOLOGISTS' CONCEPTIONS

No pathologic picture has been generally accepted among pathologists as characteristic of alcoholic gastritis. Some investigators have stated that alcoholic gastritis is not infrequently seen at autopsy. Fahr,[4] for example, stated that gastritis is often associated with so-called alcoholic cirrhosis but that there are many cases of cirrhosis without gastritis. He admitted, however, that the congestion due to obstruction of the portal system rather than the alcohol directly may be responsible for the gastritic changes. Henning[6] stated that concentrated alcohol solutions damage the glands of the stomach but that weak solutions produce hypersecretion without inflammation. Hirsch[7] examined at autopsy the stomach in 21 patients who had been heavy drinkers. Nine had died of acute delirium tremens. Zenker's fixing fluid was introduced into the stomach immediately after death in every case, and sections from all parts of the stomach were studied microscopically. These sections were compared with the original sections of the anatomist Bensley,[8] from which he described the normal microscopic picture of the adult stomach. The studies of Hirsch revealed scattered petechial hemorrhages but no consistent gastritis.

GASTROSCOPIC STUDIES

The earliest description of the living human stomach after the ingestion of alcohol was that of Beaumont[9] in 1833 concerning the fistulous stomach of Alexis St. Martin. The picture was essentially that of erythema and increase in the secretion of mucus. Only one article written since the advent of the flexible tube gastroscope could be found in the foreign literature, and none in the American literature, on the gastroscopic appearance of the stomach in a group of persons with severe chronic alcoholism. A preliminary report[2] of my alcoholic studies was made before the Chicago Society of Internal Medicine, Feb. 24, 1941. In 1936 Villaret, Moutier and their associates,[10] of Paris, studied 45 chronic alcoholic addicts gastroscopically. Each had polyneuritis and an enlarged and painful liver. Of the 45, 20 had also had ascites. All had digestive symptoms, such as increasing anorexia, bilious vomiting, constipation and diarrhea and distress after meals. Gastroscopically, all but 1 showed chronic atrophic gastritis. Fifteen patients came to autopsy, and the diagnosis of atrophic gastritis was confirmed.

My series consisted of 100 ambulatory alcoholic addicts. None of them had an enlarged or painful liver or ascites. Sixteen came to the clinic because of some type of digestive distress. The remaining 84 subjects did not seek medical aid but were induced to come to the clinic only for this study. (They are termed nonclinic addicts hereafter.) They were unattached men who lived for the most part in "flophouses" and

TABLE 2.—*Distribution of Gastroscopic Abnormalities in One Hundred Chronic Alcoholic Addicts*

	Clinic Alcoholic Addicts	Nonclinic Alcoholic Addicts	Totals
Superficial gastritis (mild)	1	34	35
Superficial gastritis (moderate)	1	17	18
Superficial gastritis (severe)	1	0	1
Hypertrophic gastritis	1	1	2
Atrophic gastritis	3	3	6
Superficial and hypertrophic gastritis	1	3	4
Superficial and atrophic gastritis	4	0	4
Erosions and hemorrhages (without gastritis)	1	3	4
Normal gastric mucosa	3	23	26
Summary			
Superficial gastritis, all forms	8	54	62
Atrophic gastritis, all forms	7	3	10
Hypertrophic gastritis, all forms	2	4	6
Erosions and hemorrhages (without gastritis)	1	3	
Normal gastric mucosa	3	23	30

"cage" hotels in the Loop district of Chicago. In their own language they were "on the bum" (table 1). They were mostly middle aged; 75 per cent were white, 24 per cent Negro and 1 per cent Mexican. Most of them

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drank in bouts of several days, remained sober for a few days and became drunk again. Others drank continuously each day. Most of them had been drinking for fifteen or more years. They consumed such varied beverages as straight whisky, beer, rubbing alcohol, home-brew, automobile antifreeze and bay rum. Whisky drinkers consumed 2 to 3 pints (a pint is 0.47 liter) per day. Some addicts drank a half gallon of wine or as much as a gallon (3.7 liters) of beer. Ninety per cent of the addicts were also heavy smokers. They were tremulous when not drinking, and many of them had delirium tremens. Cramps in the limbs rather than frank polyneuritis occurred as a rule, and hallucinations were present in some cases. The percentage of positive Wassermann reactions was not higher than that for the general population. Seven of 88 addicts had incipient tuberculosis. Nearly one half of the subjects had low grade anemia, and most of them had severe vitamin C and nicotinic acid deficiencies, as measured by the plasma ascorbic acid levels and by the porphyrin bodies in the urine. Fractional histamine tests showed achlorhydria in 7 of 56 cases. Four fifths of the men ate little or no food while drinking.

The gastroscopic picture of the 84 nonclinic alcoholic addicts was at first surprising because of the absence of gross abnormalities comparable to those seen in nonalcoholic gastritis. The one characteristic seen in all cases was a moist and glistening mucosa with increased highlights. The color was usually a uniform, evenly distributed, orange-red, which was described in 35 per cent of cases as indicative of mild hyperemia (figs. 1 and 2). The color was like that in active physiologic hyperemia rather than like the mottled or deeper red seen sometimes in chronic nonalcoholic gastritis. The disease in these cases was classified as mild chronic superficial gastritis (table 2). In 17 per cent of the cases it was classified as moderate chronic superficial gastritis, because in addition to the moist, glistening appearance the mucosa was a moderately deeper orange-red than in the first group. There were also deposits of translucent, gelatinous, gray mucus or porcelain-like white mucus between the folds in some cases. In still other cases there were scattered petechial or ecchymotic hemorrhages and tiny superficial gray erosions. The folds in some cases appeared swollen. In 26 per cent of the series the mucosa was classified as normal, but in the 35 per cent in which the disease was classified as mild superficial gastritis the mucosa presented only a little difference in color. Occasional petechial hemorrhages, erosions or small bits of mucus constituted the principal variations from normal. The low incidence of atrophic gastritis associated with widespread hypovitaminosis and subnutrition was interesting in the light of my experiences with patients with nonalcoholic gastritis. Fifty-seven per cent of all gastritis in the clinic was of the atrophic type.[2] Further, experiments strongly suggest that vitamin B complex deficiencies constitute one cause of atrophic gastritis.[2] Perhaps the more or less constant local hyperemia in the stomach of the alcoholic addict supplies adequate nutrition to the mucosal cells and thereby tends to prevent atrophy.

The 16 clinic alcoholic addicts drank at greater intervals and consumed smaller quantities of alcohol than the nonclinic addicts. Some had stopped drinking entirely for considerable periods. These patients, who were also in poor vitamin nutrition, showed a high percentage of atrophic gastritis.

SYMPTOMS

My study reveals that the heavy-drinking, nonclinic alcoholic addicts, who also smoked almost incessantly, usually had no distress after meals. In striking contrast to the clinic patients with chronic gastritis, the alcoholic addicts could tolerate all kinds of meats, baked or fried, and foods such as chile con carne and barbecue. They used large quantities of such condiments as red pepper and horse radish. Their bowels moved once or twice a day, or they had mild diarrhea rather than the constipation seen so frequently in persons with nonalcoholic gastritis. The morning nausea, or tendency to vomit, which some addicts had was prevented by what they referred to as the "eye opener," usually about a half pint of whisky. On the other hand, most of the clinic alcoholic addicts complained of intermittent dull aching around the navel, epigastric fulness, occasional nausea or vomiting. Thus, in order of the severity of their symptoms the group with nonalcoholic gastritis ranked first, the clinic group of alcoholic addicts second and the heavy-drinking, nonclinic alcoholic addicts third.

Fig. 1.—Gastroscopic view: mild chronic superficial gastritis (alcoholic type).

Fig. 2.—Gastroscopic view: normal mucosa.

Fig. 3.—Gastroscopic view: before therapy.

Fig. 4.—View after therapy.

THERAPEUTIC TESTS

In order to test whether mild inflammatory changes actually occurred, 17 chronic alcoholic addicts were given vitamin B complex and then examined gastroscopically (table 3). These tests are not reported as an experiment in therapy. Properly controlled studies along this line are now being carried out. Observations were made periodically, and the periods of therapy varied from seven days to several months. Fourteen of the 17 subjects were treated in the hospital for two to four weeks, receiving no alcohol. Gastroscopy was done every seven days. Two patients had twelve and thirteen gastroscopic examinations, respectively, over a period of three years, with intermittent courses of therapy with the vitamin B complex. After two or more weeks the gastric mucosa of the hospital-controlled patients showed a slight decrease in the orange-red and a lessening of the moist, glistening appearance (figures 3 and 4 show views of the stomach before and after therapy).

Several patients were kept on therapy a few weeks after hospitalization, during which time further reduction of the mild hyperemia and of the moist, glistening character was evident. The hyperemic color disappeared more rapidly than the moist, glistening character of the mucosa. In a few anemic patients with mild superficial gastritis the mucosa became a pale pink consistent with their reduced hemoglobin level after a few weeks of therapy. In some instances superficial gastritis superimposed on atrophic or on hypertrophic gastritis disappeared, leaving the underlying gastritic changes more prominent. After long periods of therapy atrophic changes tended to disappear also.

TABLE 3.—*Gastroscopic Diagnosis Before and After Vitamin B Complex Therapy for Seventeen Alcoholic Addicts*

Patient	Diagnosis Before Therapy	Diagnosis After Therapy	Follow-Up Period	No. of Gastroscopies
1	Superficial and hypertrophic	Superficial (mild)	1 wk.	2
2	Superficial (mild)	No superficial	1½ wk.	2
3	Superficial (mild)	Superficial (mild)	2 wk.	3
4	Superficial (moderate)	Normal mucosa	2½ wk.	3
5	Superficial (moderate)	Superficial (mild) and hypertrophic	2½ wk.	4
6	Superficial (mild)	Practically normal mucosa	2½ wk.	3
7	Superficial (mild)	Normal mucosa	3 wk.	3
8	Normal mucosa (increased highlights)	Normal mucosa	7 wk.	4
9	Superficial	No superficial; more hypertrophic	7 wk.	5
10	Atrophic	Atrophic (no change)	1 mo.	3
11	Superficial and atrophic (slight)	No superficial or atrophic (but localized hypertrophic)	2½ mo.	4
12	Superficial and atrophic	Normal mucosa	4 mo.	4
13	Atrophic	Atrophic (no change)	4 mo.	4
14	Superficial and atrophic	Atrophic (slight); no superficial	7 mo.	3
15	Superficial and hypertrophic	No superficial; hypertrophic	11 mo.	6
16	Superficial and atrophic (severe)	Mucosa practically normal	3 yr.	12
17	Superficial and atrophic	Gastritis disappeared and reappeared	3 yr.	13

SUMMARY AND CONCLUSIONS

1. The evidence from the literature on attempts to produce chronic alcoholic gastritis in experimental animals shows that in some instances a transient superficial type of gastritis has been produced but that in many other instances no gastritis has been produced.

2. Pathologists have supplied no evidence in the literature of unequivocal chronic gastritis due to alcohol. One well controlled observation (Hirsch[7]) demonstrated frequent gross and microscopic petechial or ecchymotic hemorrhages but no inflammation.

3. No previous gastroscopic study of alcoholic addicts has appeared in the American literature. The one report in the foreign literature, on 45 patients, describes extensive atrophic gastritis, which in my opinion was probably not due to alcohol directly.

4. Gastroscopic studies on 100 persons with unquestionable chronic alcoholism of long standing showed 30 per cent not to have gastritis, 35 per cent to have mild chronic superficial gastritis (with a gastric mucosa only slightly different from normal) and only 35 per cent to have unequivocal chronic gastritis.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. COHN, WHITE AND WEYRAUCH, DRS. HAMILTON AND CURTIS AND DR. BERRY

DR. SIDNEY A. PORTIS, Chicago: It is through such contributions as Dr. Berry's that we are able to reconstruct many of our ideas concerning changes produced in the stomach of patients with chronic alcoholism. All of us have thought in the past that patients with chronic alcoholism usually exhibit chronic gastritis. Many are not acquainted with the type of these patients; if one was to walk along West Madison Street in Chicago one would see the type of derelicts that were used in this experiment. If these individuals, with their debility and inanition, cannot acquire chronic gastritis after the alcohol they take, I doubt whether any one could. It is evident that we must break down some of our older concepts of disease and change some of the nomenclature. We used to talk about alcoholic cirrhosis of the liver and similarly about alcoholic polyneuritis, and yet none of us today believe that alcohol in itself is the cause of either of these two pathologic conditions. Dr. Berry produced such unusual changes in the stomach with the use of vitamin B therapy. He is conducting an excellent clinic in gastroenterology at the Provident Hospital in Chicago.

DR. DAVID J. SANDWEISS, Detroit: Drs. Hamilton and Curtis showed that hypermotility of the human stomach is associated with pylorospasm due to obstructive duodenal ulcer. I should like to ask whether hypermotility is also found associated with the epigastric distress of uncomplicated duodenal ulcer. Patterson and I have found (in a limited number of patients so far studied by the balloon-kymograph method) that epigastric pain due to uncomplicated duodenal ulcer may be present without evidence of gastric hypermotility. We have also found that the Sippy powder solution given to a patient with an uncomplicated duodenal ulcer does not inhibit gastric motility either in frequency or in amplitude of contractions or in the duration of the period of activity. Yet this solution usually gives instantaneous relief of epigastric ulcer pain. It would appear, therefore, that ulcer pains may be present without evidence of hypermotility; also that relief of epigastric distress is not necessarily associated with hypomotility. Apparently, gastric motility is not the only factor involved in epigastric or abdominal pain. How would the authors explain epigastric pain due to ulcer when normal gastric motility is present? In 1916 Ginsburg, Tumpowsky and Hamburger found that "with the onset of strong contractions the patients complained of symptoms varying in interpretation from a feeling of fulness and tightness to severe epigastric pain. The sensation nearly always came on when the contractions had reached their height." Carlson confirmed these findings but added "These contractions are not stronger or more prolonged than the stomach contraction felt as ordinary hunger pangs on days when the subject has no ulcer symptoms." I agree with Drs. Hamilton and Curtis that gastric hypermotility may be associated with certain abdominal or epigastric pains; however, one might question the conclusions drawn from the data presented. Gastric motility is modified by many afferents other than those coming from the gastrointestinal tract, such as somatic pain, physical exercise, emotional states or a cortical lesion. From a practical therapeutic point of view I believe that, while the correlation of gastric hypermotility and the organ primarily involved is of interest, therapy should be directed toward the primary focus rather than toward the hyperactive stomach. Control of the former will invariably relieve the symptoms associated with the latter.

DR. HOWARD T. KARSNER, Cleveland: The report of Drs. Cohn, White and Weyrauch adds information on an additional hazard in the use of preparations containing kaolin. Further observations are required to determine how often this complication occurs. It is possible that the patient suffered at one time from peptic ulcer, which might have permitted entry of the particulate matter into the mucosa and submucosa. It is difficult to understand the presence of the kaolin in the wall of the stomach unless there had been an interruption of surface continuity. The microscopic appearance is characteristic of the so-called pseudotubercle or foreign body tubercle. The giant cells differ from typical Langhans cells of tuberculosis in that although the nuclei are peripherally situated they are not arranged with the long axis radial to the center of the cell.

Care should be exercised not to confuse these and comparable lesions with true tubercles or miliary gummas. The experimental confirmation of the production of similar granulomas in the wall of the rabbit's stomach, together with the microchemical and microcrystallographic studies, leaves no reasonable doubt that the human lesion was due to the medicament. Of interest is the fact that polymorphonuclear leukocytes appear to have played little or no part in the reaction, especially in view of the observations of McCutcheon, Coman and Dixon on negative chemotropic effects of kaolin. As indicated by Dr. Cohn and his co-workers, information about the pathologic effects of deposits of silica is extensive. It is now known that the size or shape of the particles is of little significance in determining the lesion. Furthermore, as shown by King and Belt, the lesion is not proportional in size or character to the amount of silica within it. The lesions in the lung and spleen in silicosis are now believed to be due to silicon dioxide. The peritoneal lesions following the introduction of glove powder are evidently due to magnesium silicate. The authors have shown convincing evidence of the action of hydrated aluminum silicate in the human case and in the rabbit. The lesion differs microscopically from the usual silicotic nodule in the lung, because in the latter there is a far greater disposition to fibrosis and hyalinization than is true of the kaolin lesions. This difference may be due to variations in response to the salts present or may be due to the manner in which the lung and the wall of the stomach react. Important as is this contribution, conclusions cannot yet be drawn as to the effects of the lesion on function of the stomach.

DR. ROBY JOHN F. RENSHAW, Cleveland: I should like to ask Dr. Hamilton how long the effect of intravenous atropine lasted. With the dosage that Drs. Hamilton and Curtis gave intravenously did those patients suffer the same side effects that patients given larger doses subcutaneously or orally might suffer? There was an important point in the paper of Drs. Cohn, White and Weyrauch: the lesion was seen gastroscopically but not radiologically and not even in the gross specimen. The value of gastroscopy in this case cannot be questioned. The remarkable thing is Why don't all the people who take alcohol acquire gastritis? There must be other conditions necessary for the gastritis to develop, even though some irritant constantly insults the gastric mucosa. I shall be interested in Dr. Berry's future reports, hoping that he will observe these patients and others over a longer period of time and correlate not only the effects of alcohol but also environmental and social factors.

DR. HERMAN J. MOERSCH, Rochester, Minn.: Drs. Cohn, White and Weyrauch are to be congratulated on their ability to distinguish gastroscopically such a small lesion as a granuloma. It is especially commendable that they followed up their gastroscopic observations with experimental studies. Their experimental observations again confirm the clinical observations of Beaumont, Rogers and, more recently, Berry that the gastric mucosa under certain conditions, when exposed to an irritant, either chemical or traumatic, may give rise to an inflammatory reaction. This reaction is demonstrated easily by the local application of acetylsalicylic acid to the gastric mucosa. In some cases a region of inflammatory reaction will appear in the gastric mucosa where the acetylsalicylic acid is in contact with it, whereas in other cases such a reaction does not take place. Of even greater significance is the fact that, in those cases in which acetylsalicylic acid gives rise to an inflammatory reaction, such an inflammation is not necessarily associated with clinical symptoms. It is interesting to speculate as to whether persistent irritation of the gastric mucosa will lead eventually to further serious organic disease. This question, of course, is something that cannot be answered satisfactorily at the present time. I am especially interested in the histopathologic data concerning the changes produced in the gastric mucosa by the use of silicates. I cannot agree with the authors that both silica and silicates produce a characteristic microscopic picture in the gastric mucosa. Most observers are in agreement that silica will produce typical changes in tissue. Silicates, however, like any other foreign substance, will produce inflammatory changes but will not, as a rule, produce the characteristic fibrous nodules. It is true that asbestos and probably sericite may produce changes in tissue closely simulating those produced by silica. Although the distinction between the reaction produced in the gastric mucosa by silica and that produced by silicates may seem only of academic interest, it may be of considerable importance from a prognostic point of view.

DR. WALTER L. PALMER, Chicago: I wish to speak of the paper of Drs. Hamilton and Curtis. I found it difficult to orient myself with regard to the normal contractions. One is in the habit of seeing the so-called types 1, 2 and 3 hunger contractions, with occasional tetanic contractions, followed by periods of quiescence in a normal stomach. I am more accustomed to seeing these contractions measured with a water manometer and perhaps that is the reason it was difficult for me to orient myself. I wondered if they had taken sufficiently into consideration the differences which occur from individual to individual, that is, the normal individual and also the variations which occur with advancing age. Of course, the effect of atropine on gastric motility and on intestinal motility is well recognized. My experience has been the same as theirs in that intravenous injection of atropine does stop the contractions abruptly, but not for a very long time. Dr. Sandweiss has emphasized the fact that the seemingly definite correlation between these gastric contractions and the pain of the patient does not necessarily prove that the pain arose in the stomach. For instance, I have taken contraction tracings from the intestine and from the stomach simultaneously and found that there isn't very much lag in the intestinal contractions as compared with the gastric contractions; therefore it seems to me quite possible that the gas pains of which the patient complained really arose in the intestine rather than in the stomach, and it would seem to me quite likely, as Dr. Sandweiss suggested, that in the case of biliary colic the pain actually arose in the biliary tract rather than in the stomach. With regard to the pain of pylorospasm, Dr. Hamilton, I wish you would tell us how you diagnose that clinically. I doubt if one can.

DR. ALLAN L. COHN, San Francisco: The question as to how this material got into the mucosa, of course, occurred to us at once. We still do not know. We doubt, however, Dr. Karsner, that this man had an additional previous ulcer in this portion of the antrum where we saw the nodule. There was a diffuse infiltration of this material as far as the pylorus. We saw more areas microscopically than we did macroscopically. In the literature on the granulomas caused by talcum powder there is a report by Antopol, who demonstrated that, by rubbing talcum powder on the serosal surface of an appendix, crystals of magnesium silicate can be seen to have deeply penetrated the tissues. It is probable that this material likewise entered the gastric mucosa and caused this tumor by friction, and penetration into these scattered areas. Now, Dr. Moersch, in our paper we made no fine distinction between silica or silicates as the causative agent. We now understand from the manufacturers of the particular agent which the patient had been taking that there is a contamination in the so-called colloidal material of about 2 or 2.5 per cent of crystalline material. It is quite probable that the material consists of both the silicate and silica. The point of the paper, however, remains the same whether the foreign material is silica, silicate or both. In presenting this first case the purpose was to raise the question as to the possible irritative effect not only of kaolin but also of the whole silicate group now used in gastroenterologic practice. Our purpose was also to stress the value of gastroscopy, especially when followed by microscopic studies.

DR. FRANK E. HAMILTON, Columbus, Ohio: Our present purpose is to obtain symptomatic relief from the type of abdominal distress associated with gastric hypermotility. We have repeatedly demonstrated that atropine is the most effective drug for this purpose. There are variations in the normal motility of the human stomach. This has been emphasized by Dr. A. J. Carlson and by Dr. L. E. Barron, who was assisted by Dr. Carlson in developing the method we now use. The lantern slide used to demonstrate normal human gastric motility is from Barron's work. The variations presented by that slide are quite different from the gastric hypermotility demonstrated by the present investigation. None of the patients just presented could be classed as "normal" at the time they were studied. All of them presented a single, proved clinical entity such as

biliary colic or "pylorospasm." In such clinical conditions we have shown that the normal gastric motility is greatly altered and often resembles the Carlson type 2 or even type 3. It is not our contention that the pain necessarily originates in the stomach. Moreover, we have not stated that gastric hypermotility must be demonstrated at the time the patient experiences the sensation of pain. On the contrary we have endeavored to emphasize that when, under certain conditions, a patient complains of this type of abdominal pain we can demonstrate simultaneous gastric hyperactivity. This is particularly true of lesions involving viscera innervated by the extended vagi, as for example cholelithiasis or "pylorospasm" due to obstructive duodenal ulcer. In such instances our clinical diagnosis depends on proving at subsequent laparotomy the existence of a benign, obstructive ulcer of the duodenum. Under such conditions patients occasionally develop preoperatively certain epigastric symptoms to which the general term "pylorospasm" has been applied. At the same time we can usually demonstrate gastric hypermotility. Moreover, if the abnormal gastric hyperactivity associated with this condition can be returned to normal, the patient is simultaneously relieved of the epigastric distress. We have as yet been unable to demonstrate consistent alterations in gastric motility in patients presenting nonobstructive duodenal ulcers. We still maintain our basic conclusions that the motility of the human stomach may be regarded as an indicator of certain types of abnormal activity of the gastrointestinal tract and that control of that hypermotility will usually simultaneously control the associated symptoms.

SULFONAMIDES IN THE TREATMENT OF ERYSIPELAS

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Erysipelas, a common bacterial infection of the skin caused by the hemolytic streptococcus, is a disease entity particularly suitable for the trial of new chemotherapeutic agents. This is true because the location of the lesion makes it available for accurate study and because methods of treatment prior to the use of sulfanilamide were notably unsatisfactory.[1] In 1936, shortly after the introduction of the sulfonamide drugs, Meyer-Heine and Huguenin[2] reported 150 cases of erysipelas treated with sulfanilamide producing a rapid fall in the temperature and subsidence of the local lesion within forty-eight hours. There were no deaths and few complications. Breen and Taylor[3] in 1937 obtained equally gratifying results in 35 cases treated. There were two deaths in this series. Subsequent publications by Snodgrass and Anderson,[4] Hageman and Blake,[5] Nelson, Rinzler and Kelsey[6] and Hoyne, Wolf and Prim[7] state that the sulfonamide drugs are used with great benefit in the treatment of erysipelas, stopping the progress of the lesion, decreasing the number of days of fever and the length of hospital stay, reducing the incidence of complications and lowering the mortality rate.

Foley and Yasuna,[8] in a recent report of 80 cases treated with sulfanilamide with an equal number of untreated control cases, gave comparative results of average duration of fever of two and ninety-four one-hundredths days in treated cases and four and seventy-four one-hundredths days in the controls. The complication rate was 9 per cent in those receiving sulfanilamide and 22.5 per cent in those not getting the drug. Mortality rates were 2.5 per cent in the treated group and 10 per cent in the control series. However, Rantz and Keefer[9] considered the duration of the disease shortened only if sulfanilamide was given before the third day of the disease. They found no difference in the number of complications or in the number of relapses seen in treated cases and untreated controls.

At the St. Louis Isolation Hospital 165 patients were treated for erysipelas during the two year period between January 1939 and January 1941. All these received sulfanilamide or one of its derivatives in comparable dosage. Each patient in this series was seen by one of us. A somewhat detailed study of this group and the results of therapy is to follow.

Sulfanilamide was the chemotherapeutic agent used in 102 cases, sulfamethylthiazole in 29 cases, and a new acyl derivative of sulfanilamide, S-22, or sulfabenamide,[10] was given in 34 instances. The dosage of these drugs was as follows:

Two-tenths Gm. per kilogram of body weight up to a maximum of 8 Gm. divided into six equal doses and given every four hours for the first twenty-four hours.

Fifteen one-hundredths Gm. per kilogram of body weight to a maximum of 6 Gm. in the second twenty-four hours.

One-tenth Gm. per kilogram of body weight to a maximum of 4 Gm. daily for the duration of the hospital stay.

In addition to chemotherapy, cold boric acid packs were used routinely to relieve pain and discomfort. To prevent recurrence of the lesion, patients were hospitalized from seven to ten days and kept on drug therapy the entire time.

The age and sex distribution with mortality figures for each group are presented in table 1. It will be noted that the majority of these patients were over 40 years of age. It is well understood that erysipelas is especially fatal to the aged and to very young infants. In this series there were only 4 patients under 2½ years of age. Two of these infants, however, 9 months and 3 months of age, had extensive erysipelas that responded promptly to drug therapy.

There were 5 deaths in the group of 165, a mortality figure of 3 per cent. This compares with mortality rates of from 8 to 12 per cent before the use of sulfanilamide as reported by others.[11] Necropsies were done in 4 of the fatalities. In each instance there were complicating disease processes. These are listed in table 2.

Blood concentrations of the drug used for these patients varied between 8 and 16 mg. per hundred cubic centimeters. In each instance the local lesion was seen to regress with the treatment outlined. In case 3 the blood culture showed growth of the hemolytic streptococcus on entry but subsequent cultures produced no

1. Toomey, J. A.: Prognosis and Treatment of Erysipelas, Ann. Int. Med. **12**: 166-177 (Aug.) 1938. Hoyne, Wolf and Prim.[7]
2. Meyer-Heine, A., and Huguenin, P.: Traitement de l'érysipèle par le chlorhydrate de sulfamido-chrysoidine, Presse méd. **44**: 454-457 (March 18) 1936.
3. Breen, G. E., and Taylor, I.: Erysipelas Treated with Prontosil, Lancet **1**: 1334-1335 (June 5) 1937.
4. Snodgrass, W. R., and Anderson, T.: Sulfanilamide in Treatment of Erysipelas: Controlled Series of 270 Cases, Brit. M. J. **2**: 1156-1159 (Dec. 11) 1937. Snodgrass, W. R.; Anderson, T., and Rennie, J. L.: Sulfamidochrysoidine and Benzysulfanilamide in the Treatment of Erysipelas, ibid. **2**: 399-403 (Aug. 20) 1938.
5. Hageman, P. O., and Blake, F. G.: Clinical Experience with Sulfanilamide in the Treatment of Beta Hemolytic Streptococcic Infections, Am. J. M. Sc. **195**: 163-175, 1938.
6. Nelson, John; Rinzler, Harvey, and Kelsey, M. P.: Sulfanilamide Treatment of Erysipelas, J. A. M. A. **112**: 1044-1045 (March 18) 1939.
7. Hoyne, A. L.; Wolf, A. A., and Prim, Leona: Fatality Rates in Treatment of 998 Erysipelas Patients, J. A. M. A. **113**: 2279-2281, 1939.
8. Foley, J. A., and Yasuna, E. R.: Sulfanilamide in the Treatment of Erysipelas, J. A. M. A. **115**: 1330-1333 (Oct. 19) 1940.
9. Rantz, L. A., and Keefer, C.: Sulfanilamide in the Treatment of Erysipelas, New England J. Med. **221**: 809-813, 1939.
10. Sulfabenamide was supplied for clinical trial by Sharp and Dohme. It is 4-n-caproamidobenzenesulfonhydroxamide and is less soluble in water than sulfanilamide, 0.01 per cent going into aqueous solution. This acyl derivative had been shown to be an effective chemotherapeutic agent with low toxicity in experimental animals.
11. Toomey,[1] Nelson, Rinzler and Kelsey,[6] Hoyne, Wolf and Prim,[7] Foley and Yasuna.[8]

growth. Vegetations of bacterial endocarditis were found present in case 4. Blood cultures had been negative. In case 5 death was sudden and due to hemorrhage from a free bleeding acute duodenal ulcer demonstrated post mortem. All other deaths were due

TABLE 1.—*Age and Sex Distribution with Mortality Figures*

Age	Number	Sex	Deaths
Birth to 2½ years	4	Male..... 4	0
		Female.... 0	0
2½ years to 15 years	10	Male..... 5	0
		Female.... 5	0
15 years to 40 years	25	Male..... 9	0
		Female....16	0
40 years to 60 years	64	Male.....34	1
		Female....30	0
60 years to 70 years	44	Male.....25	4
		Female....19	0
70 years and over	18	Male.....11	0
		Female.... 7	0
Total	165		

to the complications of degenerative disease that had not responded to the usual modes of therapy. Four of the deaths occurred in the group of 102 patients who were treated with sulfanilamide, a mortality rate of 3.9 per cent. One death among 29 patients getting sulfamethylthiazole gave a 3.4 per cent mortality for this drug, while no fatalities have developed in the sulfabenamide treated series of 34 patients.

Of the 160 patients treated successfully, spread of the lesion was never noted after the first thirty-six hours of treatment. In general the erythema and induration were definitely subsiding after forty-eight hours, although some brawniness was present for from five to seven days.

In 84 cases with initial fever the temperature was normal within twenty-four hours after beginning drug therapy and remained so throughout hospitalization. Fever persisted for forty-eight hours in 49 patients, for seventy-two hours in 12, and in 4 patients for as long as four days. Thus fever persisted longer than forty-eight hours after treatment was begun in only 16 cases, or in 9.7 per cent of cases treated.

TABLE 2.—*Case Summaries of the Five Fatalities*

Case No.; Age	Color; Sex	Complicating Diseases	Drug Used	Autopsy
1 62	White ♂	Chronic nephritis, bronchopneumonia	Sulfanilamide	Yes
2 63	White ♂	Aortic aneurysm, degenerative heart disease, cardiac decompensation	Sulfanilamide	Yes
3 54	White ♂	Degenerative heart disease, auricular fibrillation, cardiac decompensation	Sulfamethylthiazole	No
4 63	White ♂	Degenerative heart disease, cardiac decompensation, bacterial endocarditis, acute glomerulonephritis, thrombosis of right pulmonary artery	Sulfanilamide	Yes
5 62	White ♂	Acute duodenal ulcer, massive gastrointestinal hemorrhage, degenerative heart disease	Sulfanilamide	Yes

Only one complication was seen in the entire series, a small subcutaneous abscess beneath the eye requiring incision and drainage. This abscess developed at the site of the erysipelas, in the region of an infected squamous cell carcinoma. There were no recurrences of erysipelas lesions.

Rantz and Keefer,[9] in their report, stated that complications occurred most frequently in those patients who did not receive the drug until late in the course of the illness. This has not been our experience. Treatment was begun with the history of the lesion existing from twelve hours to fourteen days before admission in our group of patients. Response of the individual lesion to sulfanilamide was universally prompt regardless of its duration.

As already noted, sulfanilamide was given to 102 of the 165 patients reported in this series. This drug is inexpensive but has the disadvantage of producing toxic symptoms, particularly in older persons. Nausea and methemoglobinemia were frequent. There were occasional occurrences of toxic psychoses with complete disorientation of the patient. Infrequent cutaneous rashes were seen.

Sulfamethylthiazole, although never put on the market and now prohibited from further clinical use, gave excellent results in 29 cases. It was found, in general, to be somewhat less toxic than sulfanilamide. No peripheral neuritis was seen in this small group of patients.

We have no evidence that sulfabenamide has wide applicability as a therapeutic agent. In erysipelas, however, it seems to be as valuable as sulfanilamide or sulfamethylthiazole, and in our limited experience it was gratifyingly free from toxic effects. None of

TABLE 3.—*Duration of Fever After Therapy Was Begun*

Number of Patients	Febrile Period After Beginning Chemotherapy	Percentage
84	24 hours	50.9
49	48 hours	29.7
12	72 hours	7.2
4	96 hours	2.4
16	Afebrile throughout	9.7
165		

the 34 patients had any apparent methemoglobinemia, and there were no gastrointestinal disturbances. Two morbilliform cutaneous rashes were seen but disappeared despite continuance of the drug. Mental confusion, so frequently seen in aged persons when given sulfanilamide, was not observed with this new drug.

SUMMARY AND CONCLUSIONS

1. One hundred and sixty-five consecutive erysipelas patients in the St. Louis Isolation Hospital were treated with sulfonamides, with a mortality rate of 3 per cent. Patients over 60 years of age, with chronic heart and kidney disease, furnished 4 of the 5 fatalities among this group.

2. In no instance was the lesion ever seen to spread after the first thirty-six hours on chemotherapy. A small subcutaneous abscess was the only complication. There were no recurrences.

3. In 84 patients an elevated admission temperature had returned to normal after twenty-four hours and remained normal. In 16 cases fever persisted over forty-eight hours but in no instance longer than four days.

4. Sulfanilamide was found to be fairly toxic, particularly for the aged patients in this series. The new drug sulfabenamide, used experimentally for 34 patients, produced equally good results, without the usual toxic effects so common to the sulfonamide group of drugs.

5. The prompt response of erysipelas to the sulfonamides makes this the treatment of choice and renders other therapeutic measures obsolete.

INTERSTITIAL EMPHYSEMA IN DIABETES MELLITUS DUE TO COLON BACILLUS INFECTION

REPORT OF FOUR CASES

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The development and spread of gas in the soft tissues is usually considered prima facie evidence of anaerobic gas bacillus infection.

It is not generally appreciated that colon bacilli either alone or in association with other aerobic bacteria can, in a patient with diabetes mellitus, produce interstitial gas and the severe constitutional symptoms characterizing gas gangrene.

Chiari [1] in 1893 reported the first case of the formation of gas due to colon bacillus infection in the tissues of a person with diabetes. After the death of his patient he was able to obtain pure cultures of colon bacillus from all organs, the blood and the soft tissues. Inoculation of animals with the organism failed to produce gas. Chiari therefore expressed the belief that the diabetes favorably conditioned the patient for the production of gas in the soft tissues by the colon bacillus.

Hitschmann and Lindenthal [2] in 1899 reported a similar case in which a clinical diagnosis of gas gangrene had been made. Bacteriologic studies, however, showed the absence of all anaerobes and the presence of the colon bacillus, Streptococcus pyogenes and a species of rods that could not be identified. Of these three, the colon bacillus was the only organism that produced gas on culture mediums. Hitschmann and Lindenthal concluded that the colon bacillus produces interstitial gas only in the presence of diabetes. Experimental work by them on depancreatized dogs was unsuccessful.

Warren [3] has seen 2 diabetic patients with a clinical diagnosis of gas gangrene. Repeated studies for anaerobic and aerobic bacteria, together with inoculations in guinea pigs, failed to reveal any organisms other than colon bacilli and staphylococci. Warren has observed an additional diabetic patient whose kidney was outlined by gas in a roentgenogram, but apparently the causative organism was not cultured.

Since becoming aware of the possibility of the formation of gas in the soft tissues of diabetic patients with colon bacillus infection, I have seen 4 cases of this condition within two years. It would therefore appear that the condition must be much more common than the dearth of reported cases would indicate and that it is worth while again to call attention to this manifestation of disease.

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Case 1 has been reported in detail and the report is to be published in the American Journal of Roentgenology and Radium Therapy under the title Spontaneous Renal and Perirenal Emphysema: Report of a Case in a Diabetic from Escherichia Coli Infection, by Carl L. Gillies, M.D., and Rubin Flocks, M.D.

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REPORT OF CASES

CASE 1.—E. E., a woman aged 52, entered the hospital on May 20, 1939 because of obstruction of the lower part of the urinary tract.

The patient was known to have had diabetes for the past nine years. On admission the level of blood sugar was 433 mg. per hundred cubic centimeters. The diabetes was difficult to control, and in spite of the administration of 50, 30, 35 and 25 units of insulin daily the patient passed from 26 to 80 Gm. of dextrose in the urine when receiving a diet containing 250 Gm. of potential dextrose.

An indwelling catheter was left in the bladder to relieve the symptoms of obstruction while an attempt was made to get the diabetes under control. On May 25 a severe infection of the urinary tract developed. Cultures showed only the colon bacillus.

The patient continued on a downhill course. A roentgenogram of the urinary tract taken June 20 plainly showed a small amount of gas within the parenchyma of both kidneys. On June 21 another roentgenogram (fig. 1) showed extensive infiltration of gas within both kidneys and in the soft tissues around the kidneys and the adrenal glands.

In the evening of the same day the patient was taken to the operating room and the right kidney exposed. There were a great many blebs present, and bubbles of gas escaped as the fatty capsule and the true capsule of the kidney were opened. No odor of gas could be detected. The patient went into shock and died shortly afterward.

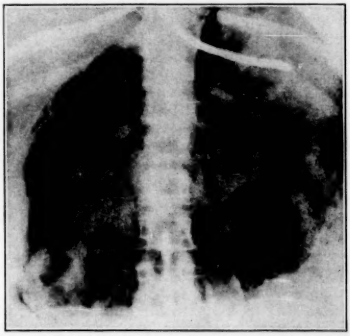

Fig. 1.—Both kidneys and adrenal glands are outlined by gas which developed within the soft tissue.

Cultures of material obtained from the right perirenal tissues at the time of operation and cultures of blood taken shortly before death showed only the colon bacillus.

CASE 2.—A. S., a man aged 63, entered the hospital on April 19, 1940 with symptoms of obstruction from a carcinoma of the rectum. On April 22 a double-barreled colostomy was done. The patient had moderate diabetes, with a blood sugar level of 420 mg. per hundred cubic centimeters on admission. Because of the operation no food was given by mouth, but 300 Gm. of dextrose without insulin was given intravenously daily. The urinary excretion of dextrose during this period varied from 6 to 53 Gm. every twenty-four hours.

The postoperative course was uneventful until the seventh day, on which signs of a severe infection developed, with a temperature of 104 F. and rapid pulse and respiration. Crepitus was observed in both thighs, and a clinical diagnosis of probable gas bacillus infection was made. A roentgenogram of the right thigh made about four hours before death showed extensive interstitial gas (fig. 2).

At postmortem examination an adenocarcinoma of the rectum that had invaded through the rectal wall was observed. Metastases were present in the liver. There was acute cellulitis

of both thighs, with crepitation extending up over the buttocks. Postmortem cultures of the blood showed colon bacilli and alpha hemolytic streptococci. Cultures of material from the peritoneal cavity in the region of the pelvis showed colon

Fig. 2.—Gas is observed within the interstitial tissues of the medial surface of the thigh and on the outer surface below the greater trochanter.

bacilli. Cultures of material from the soft tissues of the right thigh were negative for gas bacilli of the Clostridium group but gave pure cultures of colon bacilli.

CASE 3.—D. McV., a man aged 62, was admitted on June 17, 1940. He appeared seriously ill. The left foot showed a gangrenous ulcer on both the plantar and the dorsal surface extending more than halfway to the ankle. There was swelling of the ankle, with definite crepitation anteriorly. Roentgenograms confirmed the presence of gas within the soft tissues (fig. 3).

A diagnosis of diabetic gangrene with severe infection and formation of gas was made. A supracondylar amputation at the thigh was done immediately.

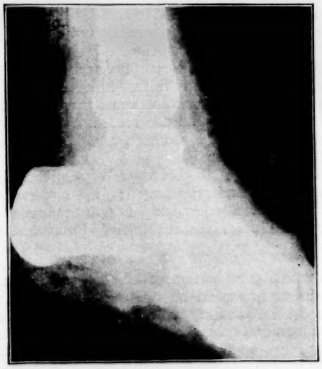

Fig. 3.—Bubbles of gas are present in the soft tissues of the plantar aspect of the foot and anterior to the ankle joint.

Cultures made from necrotic muscle of the amputated leg and foot revealed Staphylococcus aureus and the colon bacillus. Cultures for anaerobic bacteria were negative.

The patient's diabetes was not studied until after operation. When the urine was first seen there were large amounts of acetone and dextrose present. The diabetes was moderately severe, requiring for control 50 units of insulin with a diet containing 170 Gm. of potential dextrose.

The postoperative course was satisfactory, and the patient was discharged on July 14.

CASE 4.—G. W., a man aged 50, entered the hospital on Jan. 6, 1941 because of an infection of the right thigh. This had developed at the site of an injection of insulin three days before.

The patient was acutely ill. The upper part of the thigh was indurated and showed crepitus. The inguinal lymph glands were enlarged and tender. Roentgenograms showed bubbles of gas within a band of soft tissue 2.5 by 25 cm. lying below and parallel to the inguinal region (fig. 4).

The infected area was widely incised on January 6. A foul exudate and necrotic tissue were present. The odor of a colon bacillus infection was noted. Further incision was done on January 15, at which time the skin flaps were sutured back. The patient made a slow but satisfactory recovery.

Cultures of tissue obtained on January 6 showed alpha hemolytic streptococci and were negative for Welch bacilli.

Cultures of exudate taken on January 12 showed hemolytic staphylococci (Staph. aureus) and alpha hemolytic streptococci and were negative for Welch bacilli.

Because the organisms found did not explain either the presence of gas in the soft tissues or the odor of colon bacillus infection, further material for culture was obtained on Janu-

Fig. 4.—A narrow band of gas bubbles extends from the groin upward and outward to a point above the greater trochanter of the femur.

ary 21 and mediums favoring the growth of colon bacilli were used. At this time colon bacilli, hemolytic staphylococci (Staph. aureus) and anaerobic beta hemolytic streptococci were found.

This patient had known of his diabetes for eight years and before entrance had been requiring 36 units of protamine zinc insulin daily with a diet containing about 215 Gm. of potential dextrose.

When first seen in this hospital and at the height of the infection he received 36 units of protamine zinc insulin plus 45 units of regular insulin daily. On a diet of 390 Gm. of potential dextrose he excreted 42 to 52 Gm. of dextrose.

The diabetes has improved along with the infection. It is now controlled by 35 units of protamine zinc insulin plus 10 units of regular insulin daily, with the patient on a diet containing 290 Gm. of potential dextrose.

COMMENT

The ability of the colon bacillus to produce gas from culture mediums containing carbohydrates is well known. While this organism alone can probably on

occasion produce interstitial gas in a nondiabetic patient, it seems logical to assume that the presence of an increased dextrose content of body fluids and tissues offers a situation more favorable for the production of gas.

In support of this belief are the reported cases of the formation of gas in the urinary tract of diabetic patients with colon bacillus infection. It appears to be well established that at least one of the causes of primary pneumaturia is the decomposition of sugar-containing urine in the bladder by the colon bacillus.[4]

Olsson [5] reported a case in which gas was roentgenographically demonstrated in the renal pelvis of a diabetic woman who had pyelonephritis caused by the colon bacillus.

Sanes and Doroshow [6] reported 2 cases of cystitis emphysematosa with colon bacillus infection. One patient was a diabetic woman and the other an infant aged 3 months who had been receiving dextrose intravenously. These writers also noted association of an elevated sugar content of the blood with colon bacillus infection.

Marquardt [7] has recently reported another case of cystitis emphysematosa, in a diabetic woman aged 56 from whose urine were cultured the colon bacillus and Streptococcus lactis.

A most unusual case of formation of gas was reported by Reis.[8] Gas bubbles were observed in the anterior chamber of the eye of a diabetic woman with ophthalmitis thought to be due to the colon bacillus.

In diabetic gangrene not only is there an increased amount of sugar in the tissues but the impaired circulation delays absorption of any gas that may form.

In cooperation with Dr. James Greene two attempts were made to produce interstitial gas experimentally by injecting strains of the colon bacillus in the leg of a depancreatized dog whose diabetes was only partially controlled by insulin. We were unable to detect gas either clinically or roentgenographically, and the dog recovered completely from both infections. Because of the known resistance of dogs to colon bacillus infection, we do not consider the experiment comparable to similar conditions in man.

The histories of patients with true gas gangrene treated in this hospital have recently been reviewed by Bartels.[9] During the past ten years there have been 45 patients for whom the diagnosis of gas gangrene has been confirmed by the bacteriologic identification of anaerobic gas-producing bacteria. Of this group 9 were known to have diabetes. All had diabetic gangrene, but in only 1 was gas detected before amputation. In 8 the signs and symptoms of gas gangrene developed in the stump after amputation for diabetic gangrene.

CONCLUSION

With any diabetic patient showing signs of infection and the presence of interstitial gas, the possibility of colon bacillus infection should be considered first in the differential diagnosis from true gas gangrene produced by anaerobic organisms.

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HALITOSIS

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Interest in halitosis, or abnormally foul breath, has to a large extent been preempted by the oral surgeon and the rhinologist; from the references in the general literature one would surmise that it is a rare disease instead of a common condition, so little interest in the subject having been shown in the past. Every writer on the topic has emphasized the mouth, the teeth and the pharynx as sources of bad odors on the breath, attributing the fetor to decaying teeth, pyorrheal abscesses and necrotic pathologic processes in the pharynx, such as breaking-down tumors and gummas. Obviously, with the present national campaign of education and the much improved care of the teeth and the gums in children and in adults, the mouth has receded in importance as a source of bad breath; such conditions as necrotic growths are unusual and of academic interest only and play a small part. The teeth, the gums and the pharynx account for true fetor ex ore but do not explain the internal malady known familiarly as halitosis.

Our attention was attacted to this subject by the controversy which arose between two sets of observers who reported the effects of the oral administration of garlic on the exhalations of normal persons and of patients. In 1935 Haggard and Greenberg [1] reported on the feeding of raw garlic and stated that the odor of garlic on the breath resulted only from particles of the substance retained in the crevices of the teeth. When the garlic was ingested by capsule, no odor on the breath resulted. They claimed to have been able to eliminate the odor from the mouth by the use of chlorinated washes and preparations. A year or so later, Blankenhorn and Richards [2] contradicted the claims of Haggard and Greenberg. By inserting garlic via a gastrostomy tube into the stomach of a patient with complete stenosis of the esophagus, they were able to recover the odor of the garlic on the breath. With another patient, on whom tracheotomy had been performed for laryngeal carcinoma, the odor of garlic was recovered in the exhalations from the tracheotomy tube. Obviously, garlic had been absorbed by the gastrointestinal tract and its odor emitted via the lungs and the breath, even though all connection between the stomach and the mouth had been surgically eliminated.

Opposing views as to the source of a garlic odor on the breath were thus represented: (1) that the mouth and teeth are the offenders and (2) that the breath is the excretory channel of absorbable malodorous materials.

OBSERVATIONS ON PATIENT W.

An unusual combination of clinical conditions in a single patient presented an opportunity for the study of odors on the breath. This patient (W.), seriously ill with ulcerative colitis, had undergone colostomy for obstruction low in the intestine (in the middle part of the transverse colon) and ileostomy as a life-saving

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This study was assisted by a grant from the Bristol-Myers Company, of New York.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

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2. Blankenhorn, M. H., and Richards, C. E.: Garlic and Breath Odor, J. A. M. A. **107:** 409 (Aug. 8) 1936.

measure. In the latter operation the terminal portion of the ileum had been transected and both stomas anchored in the abdominal wound. In addition, the patient having a toxic psychosis, an indwelling gastric Levin tube had been inserted and was maintained in place for feeding.

The first observation of interest relates to the persistence of a strong odor of paraldehyde on the breath of the patient forty-eight hours after the administration of the drug by gastric catheter. The discharge from the site of the ileostomy was free of odor, the colon was surgically isolated and yet the odor on the breath was strong. It was a simple matter to wash out the stomach and prove that no trace of the drug remained in the gastric secretions; nevertheless for two days the odor of paraldehyde emanating from the mouth permeated the room.

The patient provided an ideal combination of conditions for the observation of other odors, particularly that of garlic, on the breath, since one could study mouth, stomach, ileum and colon as almost independent and isolated units.

The following set of simple experiments afforded a factual basis for thought and for application when directed toward the clinical explanation of true halitosis.

EXPERIMENT 1.—On April 17, 1940 at 4 p. m. the patient was given through a gastric catheter 1 cc. of concentrated extract of raw garlic (a water-alcohol trituration). There was no odor on the breath until 7:20 p. m., when the odor of garlic first became evident on the exhaled breath and in the ileostomy drainage. Evidently the odor was not present on the breath when the garlic extract was in the stomach alone but made its appearance only after the extract had reached the small intestine.

This experiment was repeated, and it could easily be demonstrated by gastric aspirations that, though the gastric content was redolent of garlic for two hours after its insertion through the tube, no odor could be detected in the mouth until the vegetable matter had reached the small intestine and presumably been absorbed.

EXPERIMENT 2.—On October 8 the patient had 3 cc. of garlic extract injected into the stomach through a Levin tube at 4:40 p. m. At 6 p. m. there was no odor on the breath but the gastric aspirate was definitely odorous of garlic. At 6:40 and 7:30 p. m. the breath was strong in garlic odor, as was the ileostomy drainage.

On October 9 at 8 a. m. the odor had persisted on the breath and in the ileostomy drainage after sixteen hours; the gastric aspirate had no odor after sixteen hours. At 6 p. m. the odor on the breath was still fairly strong, but there had been none in the ileostomy drainage or in the stool since 8 a. m. after twenty-six hours.

On October 10 at 9 a. m. the odor of garlic was still present on the breath (after forty hours); it persisted until 2:30 p. m. (forty-five and one-half hours altogether). At 5 p. m. (after forty-eight hours) there was no odor on the breath.

The garlic odor on the breath was not present in the first hours, even though garlic could be demonstrated by aspiration to be residual in the stomach, but was present long after the gastric aspirate was free of garlic. The odor persisted in the mouth more than twenty-four hours after the stomach, ileum and colon were shown to be free of a persistent residue of garlic.

EXPERIMENT 3.—On October 11 the patient had 5 cc. of garlic extract injected into the distal loop of the ileum at 9:45 a. m. By 10:45 a. m. a faint odor had appeared on the breath; it was still present though faint at 5 p. m.

Apparently absorption from the distal part of the ileum and the colon does take place, and the substance is excretable on the breath. (The constant diarrheal movements of the patient probably interfered with full absorption.) The stomach, the upper part of the ileum and the jejunum play absolutely no part.

When experiment 3 was repeated, with the garlic inserted into the proximal loop of the ileum, prompt absorption was demonstrated by the appearance of the odor on the breath within three hours.

EXPERIMENT 4.—In order to ascertain the role of the teeth and the mouth as isolated organs in maintaining a characteristic odor, the anterior and posterior surfaces of the patient's teeth and the interstices were painted with a strong garlic extract by means of a camel's hair brush, no saliva being swallowed. For one hour only there was a strong garlic odor on the breath; soon thereafter no odor was detectable.

To check up on the foregoing surprising observation, a normal person was asked to chew some strongly garlicized salami, swallowing none of it and expelling all his saliva. Large particles of salami were driven into the interdental spaces. The immediate odor on the breath was powerful, but within an hour only a faint odor remained, and within two hours no odor of garlic was detectable.

EXPERIMENT 5.—Whisky, instead of garlic, was employed in order to evaluate the role of the mouth alone in halitosis. Normal persons were asked to rinse the mouth and teeth with strong rye whisky, swallowing being suspended during the operation. The whisky odor was retained on the breath only twenty to thirty minutes.

A normal person introduced into the fasting stomach a Levin tube, then rinsed the mouth and teeth with good rye whisky and swallowed an abundant amount. Immediately the ingested whisky was siphoned out of the stomach and the gastric chamber washed with warm water. Within twenty minutes even the slightest whisky odor had disappeared from the breath.

These experiments were repeated on the psychotic patient W. When whisky was injected through the Levin tube, care being taken to avoid all contamination of the mouth, no odor was immediately apparent on the breath, though by repeated aspirations of the gastric contents the whisky was shown definitely to have been retained in the stomach. At no time did a whisky breath become evident; presumably the quantity necessary to produce an alcoholic breath far exceeds the therapeutic dose, and apparently the whisky must first be absorbed.

GROUP OBSERVATIONS

A more extensive study of garlic and other odorous substances was undertaken with large numbers of hospital patients in order to trace the path of absorption, excretion and exhalation of such substances. Patients with a jejunostomy, ileostomy or colostomy opening, a short-circuiting anastomosis, a gastrojejunocolic fistula or pyloric stenosis were utilized, as well as many subjects who had undergone resection of a segment of the small intestine or partial or complete colectomy.

Raw chopped garlic was enclosed in double gelatin capsules for oral administration, and the same capsules were used for insertion into various bodily apertures, natural and artificial. The dose of garlic ranged from 0.5 to 1 Gm.; however it was administered, a latent period of one-half to one or two hours ensued, during which no odor on the breath was demonstrable; thereafter a strong odor occurred, which lasted for four to twenty-six hours and then tapered off to a musty faintness. Children were found most susceptible to small doses; women were much more susceptible than men. The garlic was absorbed from all parts of the intestinal tract, large or small, regardless of the extent of the resection which had been performed. No garlic seemed to be absorbed from the stomach in cases of complete pyloric stenosis. If belching or vomiting took place

while the stomach contained garlic, the odor was immediately apparent on the breath. As long as the cardia acted as an effectual valve, no odor could be observed.

Once the garlic was in the intestine, cathartics and enemas were ineffectual in ridding the intestine and the breath of garlic odor. One or two doses of a saline cathartic were eventually effectual if the amount administered was sufficient and the effect obtained soon enough after ingestion.

When garlic and indigo carmine were inserted into a jejunostomy opening, the odor appeared on the breath in one-half hour and persisted for nineteen hours; during that whole period the indwelling gastric catheter proved that none of the material had been regurgitated into the stomach. Evidently the mechanism of reverse peristalsis plays little part in the production of garlic halitosis, a fact which has much negative significance in the interpretation of the meaning of true halitosis.

ROLE OF THE LIVER AND BILE IN THE TRANSMISSION OF GARLIC ODORS

It was at this point apparent that garlic halitosis depended on absorption of the material from the intestine and was independent of an oral or a gastric mechanism. But it was also noted, by observations made on patients with various intestinal stomas, that long after the garlic odor had disappeared from ileac or colonic washings and drainage fluids the oral odor persisted. One of our earliest observations was that the ileostomy drainage ceased to smell of garlic after seven hours but that the breath gave off the odor for fully forty hours longer.

Where in the body was the garlic being stored? Naturally our first thought was the liver, one of whose functions is the storage and detoxification of foreign materials. We were able to utilize in our experiments 3 patients with carcinoma of the pancreas and complete obstruction of the bile passages in whom biliary drainage had been surgically established. When 0.5 Gm. of garlic (in a capsule) was administered by mouth the typical garlic odor was detectable in the bile within one or more hours. The same held true when the garlic was administered by rectum. The odor in the bile persisted for fifteen hours; on the breath it lasted twenty-five. In another experiment a saline cathartic was given six hours after the ingestion of garlic; the laxative failed to have effect, since the odor persisted in the bile for twenty-two hours and on the breath for twenty-four. Odor in the bile and odor on the breath appeared almost simultaneously, but that on the breath always persisted for one to two hours after the bile had ceased to be malodorous. Once the bile drainage became redolent of garlic, it was not possible to drive out the odor by the use of saline laxatives or to shorten its expected duration. We should like to have tried the effects of mild mercurous chloride or choleretics on the duration of the garlic odor in the bile, since it seems logical that a true choleretic would materially curtail the duration of such an odor. There has not been sufficient opportunity or time for all the experiments which suggest themselves. However, this much is true: After the liver cleaned itself of the garlic odor, the breath followed suit within a few (usually only two) hours.

OBSERVATIONS WITH VOLATILE SUBSTANCES

Many of the experiments in which garlic had been employed were repeated with oil of peppermint and oil of wintergreen in order to ascertain some simple facts. We wished to know whether other volatile odorous substances travel the same route from intestine to liver to lungs and to breath and whether such pleasant odorous matters are exhaled on the breath. In general, the volatile oils of peppermint and wintergreen acted exactly as had garlic. Children and women excrete peppermint on the breath when it is given in moderate doses; men excrete it with less facility and only when it is given in much larger amounts. Oil of wintergreen is much less potent than peppermint, large doses being necessary to produce the odor on the breath. When peppermint and garlic were given simultaneously it was not possible completely to mask the garlic odor even by large doses of peppermint oil. The odor of peppermint could be recovered from the bile drainage of patients with cholecystectomy openings when the oil had been administered either orally or rectally. With the oral dose, the odor on the breath lasted one to six hours; with the rectal dose, the odor persisted in the bile only one to two hours.

During these experiments we observed a patient suffering with diffuse eczema of the trunk and the extremities, to which liberal applications of a mentholated ointment had been applied to allay the pruritus. The breath of this patient smelled strongly of menthol. This fact should not seem unusual, since it has been known that oil of garlic applied to the soles of the feet of a child can give rise to garlic breath.[3] We were easily able to reproduce this simple phenomenon of cutaneous absorption and exhalation on the breath with pure oil of garlic applied to the skin of a child.

Skatole and indole were investigated because they had long been considered important intestinal factors underlying true halitosis. Indole, in doses of 25 to 250 mg., was administered by mouth (in capsule form) to patients of various ages and of both sexes. With the larger doses, several persons had toxic symptoms of nausea and lassitude; the odor of indole usually appeared on the breath one hour after ingestion, and it endured for one to thirteen hours. It could be easily overcome by administering oil of peppermint.

The ingestion of skatole in capsule form creates a peculiar musty odor not unlike that of true halitosis but weaker and of shorter duration than the odor caused by indole or the other volatile substances used in experiments.

COMMENT AND CLINICAL APPLICATION

What relation do the interesting pharmacologic observations mentioned bear to the elucidation of the problem of true halitosis?

Unless pathologic oral or nasopharyngeal conditions exist, the mouth, the teeth and the pharynx play little or no part in the production of essential halitosis. Nor, for that matter, does the stomach play a part, for it can easily be shown that with a perfectly functioning cardiac sphincter, malodorous substances introduced into the stomach do not, by their mere presence, taint the breath. One can verify this point by smelling the breath of patients with pyloric stenosis, whose gastric content is always rancid and malodorous. Providing neither vomiting nor belching has recently occurred, the breath of such patients is not redolent of the characteristic vile-smelling gastric residue.

A patient with gastrojejunocolic fistula was observed; the fistulous tract was large and broad and had established itself between the transverse colon and the stomach. When the patient belched, a vile fecal odor was apparent on the breath; otherwise halitosis was absent.

3. Silverstine, C. T.: Garlic Breath Odor, Ohio State M. J. **32**: 1232 (Dec.) 1936. Pechey, John: The Compleat Herbal of Physical Plants, ed. 2, London, 1707.

Obviously the intestines, large and small, are the critical points, for the mucosa allows the absorption of noxious materials, their transport to the liver and their further migration, apparently by way of the circulation, to the lungs and thence to the breath. That this is the route traversed by garlic can be easily demonstrated. We have traced the garlic as far as the liver and the biliary excreta. That garlic is and can be carried in the blood stream has been shown by Goodman and Beargd,[4] who demonstrated on the breath of newborn infants the odor of garlic which had been ingested by the mother before delivery. Since the only method of transference would be for substances to pass from the maternal circulation through the placenta to the fetal circulation, it must be assumed that the blood can carry garlic in solution. The lungs function as an organ of excretion, withdrawing volatile materials from the circulating medium and exhaling them on the breath. Similarly, when paraldehyde is injected intravenously the odor appears rapidly on the breath and persists for forty-eight hours.

Let the hypothesis be made that essential halitosis is the excretion on the breath of malodorous fats, fatty acids or volatile substances resultant from some fault in the digestion or metabolism of fat. The noxious volatile matter is absorbed from the intestinal tract (probably from the lower part of the ileum), is carried to the liver (where insufficient or ineffectual neutralization or detoxification ensues), is partly excreted in the bile but in the main is picked up by the circulating blood, which in traversing the alveoli of the lungs parts with the substance, which is exhaled on the breath. What clinical facts can be brought forward to substantiate such a hypothesis? It has been noted that the Chinese strenuously object to the body odor of white persons and attribute that odor to the milk and butter which Caucasians so freely ingest (Snapper).[5] Caucasians are said by the Chinese to smell of "cow." We have observed that patients with ulcer given a Sippy diet or, particularly, treated by the continuous milk drip method frequently have true halitosis. If such patients are given a diet of cereal, eggs and lean meat—a diet of low fat content—the typical odor disappears. If a high fat diet containing butter and milk is reinstated, the halitotic odor will readily recur.

Patients suffering from true halitosis are similarly amenable to the therapeutic test of a low fat diet. If a reducing diet, low in fats (40 to 60 Gm. a day), is administered, a prompt disappearance of the halitotic odor occurs.

Our clinical observations are as yet too few and too recent to allow us to make our hypothesis a categoric statement, but the therapeutic suggestiveness of the procedure seems promising.

A direct attack on the intestine and the liver should also merit attention, for these are the sources of the disagreeable odor. A single moderate dose of a saline laxative does not clear up halitosis. If the laxative is given daily in larger doses, the oral odor is much ameliorated.

Colonic irrigations are less effectual in reducing the oral fetor, a fact which makes us believe that the small rather than the large intestine is the sink of iniquity. Constipation in itself seems to play little part in the production of halitosis.

What part the liver plays remains at this point conjectural. We were unable to drive out the odor of garlic from the bile by the use of saline laxatives or cathartics, but, again, insufficient time and experiments preclude final deductions. Perhaps a true choleretic would serve such a useful purpose successfully.

It would be alluring to think of covering a true halitotic odor by the administration of oil of peppermint or oil of wintergreen. If the oil were ingested in sufficient amount, the exhaled odor might within two to three hours overcloud the halitotic odor and replace it with a less noxious if not an agreeable one.

Mouth washes containing pleasantly odorous materials serve to hide or mask true halitosis as a temporary measure but fail completely to meet the problem, since the source of the fetor is in the intestine and the metabolism. A true attack on the problem must be directed to the fatty or volatile constituents of the diet and their elimination via the liver, the intestinal tract and the lungs.

This report is intended as a preliminary rather than as a finished study. The amplification of our hypothesis and its tentative implications in the study of large numbers of patients with true, or essential, halitosis would require considerable time, patience and accurate observation. Methods of precision and titrimetric estimations of odors have in our hands proved less satisfactory than the direct use of the nose. The clinical application of our hypothesis to the study and elimination of essential halitosis should readily prove the theory of the intestinal origin of halitosis and the hepatic storage of halitotic agents, or the theory should be corrected and revised by additional facts and observations.

1075 Park Avenue.

4. Goodman, Louis, and Bearg, Phillip: That Garlic Odor, J. A. M. A. **108:** 136 (Jan. 9) 1937.
5. Snapper, I.: Personal communication to the authors.

THE ORAL MANIFESTATIONS OF VITAMIN DEFICIENCIES

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As the main system for the ingestion and absorption of foodstuffs, the gastrointestinal tract occupies a prominent position in the causation of vitamin deficiencies. Thus it has been pointed out that "any pathologic condition which interferes with normal food intake, normal digestion, normal absorption of the products of digestion, and normal utilization of these products by the liver, may produce secondary or conditioned avitaminosis."[1] In addition, the gastrointestinal tract is one of the first systems to present objective clinical signs when deficiencies of certain vitamins occur.

An examination of the diets usually prescribed for patients with peptic ulcer, colitis and disease of the gallbladder shows that they often consist mainly of refined carbohydrate and are apt to be deficient in one or more of the vitamins. Patients with idiosyncrasies regarding food expressed in the diet they select will more often than not favor refined foods low in vitamins. On the

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Studies on which this paper is based were aided by grants from the John and Mary R. Markle Foundation, the Dazian Foundation for Medical Research, the Williams-Waterman Fund of the Research Corporation and the Nutritional Research Fund of the Medical Service of the Psychiatric Division of Bellevue Hospital.

1. Mackie, T. T.; Eddy, W. H., and Mills, M. A.: Vitamin Deficiencies in Gastrointestinal Disease, Ann. Int. Med. **14:** 28 (July) 1940.

other hand, even when the prescribed or self-selected diet is adequate in vitamin content, medication may destroy the vitamins contained in the ingested food or interfere with their absorption. In the presence of alkalis vitamin C, thiamine, riboflavin and perhaps other vitamins are inactivated. The use of active colloidal adsorbents, such as magnesium trisilicate, aluminum hydroxide and mixtures of these two, in the treatment of peptic ulcer raises the problem as to the amount of vitamins, particularly the water-soluble vitamins B and C, that is adsorbed onto these compounds and excreted without being utilized. This is more than speculation, because such adsorbents are extensively utilized in the isolation and purification of many biochemical substances, including the vitamin B components. Anderson [2] has demonstrated that the ingestion of liquid petrolatum along with vitamins A and D will cause solution of the vitamins in the oil, with their resultant excretion and nonutilization.

From the surgical aspect, the liberal use of fluids parenterally in the form of solutions of dextrose has contributed a great deal to the production of subvitaminosis B in patients who have undergone operative procedures on the gastrointestinal tract. The same danger prevails in other states in which parenteral feeding is resorted to for any reason. The excessive amounts of vitamin-free carbohydrate quickly deplete the body's meager stores of the vitamin B complex, and deficiency symptoms appear after several days of parenteral feeding with dextrose. So-called water intoxication, attributed to the excessive administration of fluids parenterally, may often be actually the syndrome of wet beriberi and may respond rapidly to the administration of thiamine hydrochloride in adequate amounts. Production of nicotinic acid deficiency and perhaps deficiency of other components of the vitamin B complex may also follow the prolonged parenteral use of carbohydrate. Hence it is a wise prophylactic measure to administer thiamine hydrochloride, riboflavin and nicotinic acid to all patients receiving fluids parenterally, either by giving the substances separately or by including them in the dextrose solutions.

Among the principal causes of deprivation of vitamins despite an adequate intake are the diarrheal states, especially when of long duration, as in cases of colitis, sprue and intestinal tuberculosis. Dann and Cowgill [3] have demonstrated that the experimental production of diarrhea in dogs considerably increases their requirement of thiamine. The diarrheal factors and the manner in which they produce vitamin deficiencies were discussed in a recent paper by Bean and Spies.[4] They emphasized besides the mechanically increased loss due to rapid passage of the intestinal contents through the body, such other factors as failure of the normal enzymic breakdown of foods because of the decrease or absence of the digestive secretions and the prevention of absorption caused by anatomic changes associated with chronic intestinal disease and diarrhea, such as scarring, induration or inflammation of the intestinal wall. They suggested, in addition, that the phosphorylation of foodstuffs, which is necessary for the activation of vitamins and which takes place in the intestine, is probably interfered with in diarrhea. Lastly, they pointed out that fever, which coincidentally increases the metabolism and the requirement of vitamins, and symptoms such as nausea and pain reduce the intake of food, with consequent limitation of the intake of vitamins.

From the foregoing remarks one may realize the importance of the gastrointestinal system in the body's vitamin economy, not only as the main route for the introduction of vitamins but also as the means of elution from foodstuffs, absorption and transformation into active forms. The possible development of deficiency states in patients with gastrointestinal disorders must be carefully evaluated, since the onset of a deficiency syndrome usually provokes a vicious cycle; in vitamin B deficiency the absorbing and utilizing powers of the alimentary tract are interfered with, and this progressively exacerbates the symptoms of deficiency. Administration of the entire vitamin B complex and, in addition, any of the synthetic factors, as indicated, is of prophylactic value in all cases of disease of the gastrointestinal tract. In the absence of simple and rapid laboratory tests for vitamin deficiency states, the importance of recognizing the oral manifestations of vitamin deficiency is obvious.

Lesions of the lips, gums, tongue and buccal mucous membranes are characteristic of deficiency of vitamin C and of several members of the vitamin B complex. Response to specific therapy is mirrored rapidly by changes in these lesions. We believe therefore that these early and characteristic phenomena may be used not only in diagnosis but for the evaluation of therapy.

Characteristic oral lesions are commonly observed in deficiency of vitamin C, or scurvy. These, however, are rarely isolated and are usually colored by the presence of other deficiencies. As the function of vitamin C is concerned with the formation and regulation of the intercellular matrix, the gingival lesions are due to a vascular diathesis which produces swollen and boggy gums that bleed easily and progress to actual ulceration. Chewing is difficult, and involvement of the alveolar bones causes the teeth to loosen and fall out. The teeth themselves may be affected by the scorbutic process, the dentin and enamel becoming porous and defective, with resulting rapid and early decay. Hemorrhage into the buccal mucosa may result from the damage to the vascular epithelium.

Investigations thus far have disclosed no oral lesions characteristic of thiamine deficiency. Characteristic stomatitis and glossitis are diagnostic of nicotinic acid deficiency.[5] These appear early in the course of the disease as swelling and redness of the tip and the lateral margins of the tongue. With the progression of the disease, the reddening becomes more intense until these parts assume a fiery scarlet hue. At the same time ulcerations appear along the sides, the tip and the under surface of the tongue and on the buccal mucosa, particularly opposite the molar teeth. These ulcerations are frequently covered with a thick grayish exudate or membrane in which Vincent's organisms can be found. The response to adequate nicotinic acid therapy is often dramatic. Blanching of the fiery redness usually occurs within twenty-four hours, and healing of the ulcerations may be noted in forty-eight to seventy-two hours.

2. Anderson, Oluf: Influence of Liquid Petrolatum on the Absorption of Vitamin A, Acta paediat. **24**: 422, 1939.

3. Dann, Margaret, and Cowgill, G. R.: Influence of Diarrhea on the Vitamin B_1 Requirement, Arch. Int. Med. **62**: 137 (July) 1938.

4. Bean, W. B., and Spies, T. D.: Vitamin Deficiencies in Diarrheal States, J. A. M. A. **115**: 1078 (Sept. 28) 1940.

5. Spies, T. D., and Cooper, Clark: The Diagnosis of Pellagra, Internat. Clin. **4**: 1 (Dec.) 1937.

Gastrointestinal, mental and cutaneous changes which may be present may not manifest equally dramatic response to treatment.

The first distinct clinical picture in man attributed to deficiency of riboflavin was demonstrated experimentally by Sebrell and Butler,[6] who, by maintaining 18 women with the diet of Goldberger and Tanner, experimentally produced oral pallor followed by maceration and superficial transverse fissuring in the angles of the mouth. These lesions resembled those described as perlèche. At the same time a superficial denudation of the mucosa caused the lips to become abnormally red along the line of closure. "In addition to the cheilosis there was also seen a fine, scaly, slightly greasy desquamation on a mildly erythematous base in the nasolabial folds, on the alae nasi, in the vestibule of the nose and on the ears." Under the conditions of the experiment these lesions were alleviated by the administration of synthetic riboflavin but not by nicotinic acid. Since then this deficiency has been found prevalent as a spontaneous condition.[7] Kruse, Sydenstricker, Sebrell and Cleckley[8] have reported, in addition, a keratitis associated with these signs of riboflavin deficiency in 10 subjects.

We[9] have reported on 15 subjects having lesions due, we believe, to ariboflavinosis. In addition to the riboflavin deficiency, 13 had nicotinic acid deficiency, 7 had vitamin B_1 deficiency and 3 had vitamin C deficiency, all clinically manifest. Only 1 patient showed no clinical evidence of another vitamin deficiency. Since then, however, we have observed innumerable subjects, including university students, nurses, dietitians and persons with high incomes, who presented a cheilosis that responded to riboflavin but who showed no clinical evidence of another deficiency disease. It is our belief that ariboflavinosis is the most common isolated deficiency that is objectively manifest.

The facial lesions seen in our cases of riboflavin deficiency consisted of filiform, seborrheic excrescences, in length up to 1 mm. apparently derived from the sebaceous glands and closely to sparsely scattered over the skin of the face. Their characteristic location was in the nasolabial folds, but they occurred frequently on the alae nasi, occasionally on the bridge of the nose and sometimes on the forehead above the eyebrows. The skin on which the excrescences were located was the seat of a fine, scaly, greasy desquamation. On casual inspection these filiform lesions resembled urea frost, but they could not be brushed off by rubbing with the fingers. In addition, most of the patients showed fissures and maceration at the angles of the mouth and a degenerative crustlike formation on the epithelium of the lips, most evident on the lower. The fissures occurred in both angles of the mouth and extended laterally 1 to 3 mm. onto the mucous membrane of the mouth and 1 to 10 mm. onto the skin. They were usually shallow but were sometimes 0.5 mm. deep, and their bases as a rule showed little or no increased redness. In an area extending for 5 to 20 mm. from the angle of the mouth onto both lips, the mucous membrane was macerated, wrinkled and pearl gray. The lips, particularly the lower one, frequently showed a decided increase in the vertical fissuring, often without a break in the mucous membrane. Occasionally the vestibule of the nose was involved, with lesions similar to those on the lips.

The polymorphous nature of the lesions of the tongue and mouth found in patients with frank nicotinic acid and riboflavin deficiency is illustrated by the experience of having the affected areas, particularly the tongue, return to a normal texture and color only after the entire vitamin B complex, or a good diet containing its components, has been administered. Among the patients who still presented stomatitis and glossitis after treatment with nicotinic acid and riboflavin were a number in whom the tongue was smooth, slightly edematous and of a peculiar purplish or magenta hue. Often these patients complained of pain in the tongue. The tongue would return to normal after a sufficient amount of the whole vitamin B complex had been given. With the isolation and synthesis of vitamin B_6, or pyridoxine, it became possible to differentiate a lesion of the tongue that is probably due to a deficiency of this vitamin. The following case history illustrates this type of lesion and the manner in which it originates.

REPORT OF A CASE

D. R., a white woman aged 31, was admitted to our service in March 1940 because of emotional disturbances, with irrationality. There was a history of headaches, fatigue and weakness for two weeks and prolonged heavy drinking. The patient was confused and disoriented. There was bilateral nystagmus. The tongue and buccal mucous membranes were normal. There was no nasolabial dermatitis or cheilosis. The skin and the conjunctivas were moderately icteric. Palpation of the abdomen disclosed that the edge of the liver was firm at the level of the umbilicus, with prominent lateral abdominal veins but no evidences of fluid. The heart and lungs were without significant abnormalities. Treatment with nicotinic acid, ascorbic acid and vitamin A was instituted, while the patient was maintained with a basal diet.

The mental condition slowly improved, but on the third day the patient complained of soreness of the tongue. On examination the tongue was found to be somewhat smooth, most obviously about the edges, and purple-red, or magenta. The lower lip also was of this color, though there was no cheilosis. Thiamine hydrochloride was added to the therapeutic agents, the daily dose of nicotinic acid was increased to 1,000 mg. given orally in divided doses and 200 mg. of sodium nicotinate was given intravenously. This caused no change for the better in the tongue and lips; if anything the magenta coloring of the tongue was intensified, and the patient claimed that her tongue was becoming increasingly painful. On and after the eighth day of the foregoing regimen she was given, in addition, 100 mg. of pyridoxine hydrochloride (vitamin B_6) daily by intravenous injection. By the second day of treatment the soreness of the tongue had almost disappeared and the color had become distinctly lighter. On the fourth day the tongue was almost normal in color, with evidence of new papillae about the center area, which was still somewhat redder than normal. The following day the color had blanched further, and there was definite beginning regeneration of papillae. The lips also at this time had returned to an almost normal color.

The progressive production of characteristic glossitis in a patient maintained with a diet low in the vitamin B complex and supplemented by nicotinic acid, thiamine,

6. Sebrell, W. H., and Butler, R. E.: Riboflavin Deficiency in Man: Preliminary Note, Pub. Health Rep. **53**: 2282 (Dec. 30) 1938.
7. Oden, L. H., and Sebrell, W. H.: Report of Three Cases of Ariboflavinosis, Pub. Health Rep. **54**: 790 (May 12) 1939. Sydenstricker, V. P., cited in Jolliffe, Norman: Clinical Aspects of Vitamin B Deficiencies, Minnesota Med. **23**: 542 (Aug.) 1940.
8. Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H., and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis, Pub. Health Rep. **55**: 157 (Jan. 26) 1940.
9. Jolliffe, Norman; Fein, H. D., and Rosenblum, L. A.: Riboflavin Deficiency in Man, New England J. Med. **221**: 921 (Dec. 14) 1939.

ascorbic acid and vitamin A and the rapid improvement and return to normal of the tongue when vitamin B_6 was administered constitute, we believe, experimental evidence of a vitamin B_6 (pyridoxine) deficiency.

We have observed, in addition, a stomatitis characterized by the persistence of redness of the mucosa and the presence of many small plaques, looking like milk curds, which could not, however, be washed or rubbed off the mucous membrane. The exact nature of the deficiency causing the stomatitis is not known. We have found this condition in pellagrins as a residuum after the stomatitis due to nicotinic acid deficiency had been healed. It does not respond to treatment with vitamin B_6, riboflavin or nicotinic acid, singly or in combination. Restoration of the mouth to normal was accomplished only after intensive therapy with the vitamin B complex. The factor or factors responsible are present in the vitamin B complex and may be any of the less well known fractions which have not as yet been isolated or synthesized and consequently have not been applied in human nutritional studies.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. CROHN AND DROSD AND DRS. ROSENBLUM AND JOLLIFFE

DR. THOMAS T. MACKIE, New York: Drs. Rosenblum and Jolliffe brought out a fact which needs constant emphasis: that many of the diets which we use in the clinical management are deficient from the point of view of nutrition. I should like to interject a note of caution about the too rigid interpretation of a particular sign and its association with deficiency of a particular crystalline product. I have seen instances presenting the physical signs said to be characteristic of ariboflavinosis that have not responded to heavy dosage of riboflavin until that was supplemented by large doses of brewers' yeast; furthermore, the nasolabial lesions which are described as resulting from ariboflavinosis in the hands of other observers have been described as clearing promptly, within a matter of four or five days, on the administration of nicotinic acid as well as of riboflavin. There is a possibility that the function of these specific factors is interrelated chemically and that the exhibition of one particular substance may lead to the clearing of a particular physical sign, not as a result of the specific action, but as the result of some improvement in general intracellular metabolism. The therapy that I employ whenever I deal with a proved or suspected avitaminosis must recognize that the most important agent is a properly balanced diet and that at the present time the field of usefulness of crystalline products is limited to the meeting of specific indications. One cannot use the shotgun preparations as a substitute for a proper dietary.

DR. W. H. SHEALY, Sharpsburg, Md.: I should like to ask about the treatment of pure Vincent's infection.

DR. LOUIS A. ROSENBLUM, New York: In the treatment of Vincent's angina with nicotinic acid it is important to differentiate between the presence of fusiform bacilli and spirochetes associated with the characteristic nicotinic acid deficiency stomatitis and the true or so-called dental Vincent's angina, which has a typical pseudomembrane and is without the fiery red appearance of the mucous membranes that is so characteristic of nicotinic acid deficiency. Probably the impaired tissue oxidations and other metabolic disturbances that occur in the presence of a deficiency of nicotinic acid provide the approach to the anaerobic environment apparently necessary for the proliferation of the Vincent's organisms; with return of the tissues to a normal metabolic status by the administration of nicotinic acid the organisms disappear and Vincent's angina is cured. But true Vincent's angina not associated with a nicotinic acid deficiency stomatitis does not usually respond to treatment with nicotinic acid.

Clinical Notes, Suggestions and New Instruments

INTERSEXUALITY PROVED BY OPERATION AND MICROSCOPIC EXAMINATION

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It is becoming more widely accepted, as science progresses, that there are few persons who are either wholly male or wholly female but rather that there is a little of the female in all men and a little of the male in all women. The ratio may sometimes be unduly exaggerated and far from the usual normal proportions, which may make it difficult at times to determine whether the individual is basically a male or a female. For this kind of person the term "intersex" has been coined. The case reported here presents one of these problems of intersexuality.

It is not within the province of this report to enter into the theories of formation, suggested mechanisms, hypothetic

Fig. 1

Fig. 2

Fig. 1.—Appearance of patient a few years before being seen by us.
Fig. 2.—Appearance of patient two months prior to operation. Note absence of pubic hair. The breasts and breast areolas simulate pregnancy as a result of estrogenic therapy.

causative factors or reports of the various classifications of intersexes. For those interested in recently proposed theories and collective reviews of the subject, suitable references are offered.[1] Here, the statement should suffice that immediately

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1. von Neugebauer, F. L.: Hermaphroditismus beim Menschen, Leipzig, Dr. Werner Klinkhardt, 1908. Hirsch, E. W., and Jones, T. G.: A Case of Pseudohermaphroditism in Which Operation Was Performed for Undescended Testes, J. A. M. A. **92**: 2018 (June 15) 1929. Allen, Ezra: Sex Reversal and the Basis of Sexuality, J. A. Inst. Homeop. **25**: 908 (Aug.) 1932. Huggins, R. R.; Cohen, M., and Harden, B.: True Hermaphroditism in a Man, with an Endocrinologic Study, Am. J. Obst. & Gynec. **34**: 136, 1937. Young, H. H.: Genital Abnormalities, Hermaphroditism and Related Adrenal Diseases, Baltimore, Williams & Wilkins, 1937. Rubovits, W. H., and Saphir, William: Intersexuality, J. A. M. A. **110**: 1823 (May 28) 1938. Charvat, J.; Kodicek, E., and Schubert, O.: Clinical, Hormonal and Histological Conditions in a Case of Hermaphroditism (Fem. Ext.), Endocrinology **23**: 91, 1938. McCabey, J. F.: A New Concept of Hermaphroditism, Surg., Gynec. & Obst. **67**: 646, 1938 (contains a review of 67 reported cases to date); The Sexes

[Footnote 1 continued on next page.]

after spermatozoal impregnation of the ovum the union and fusion of definite types of chromosomes at once determine the genetic sex of the future individual. (For example, when a spermatozoon containing an x-chromosome fuses with an x-chromosome of the ovum, a potential female offspring may be

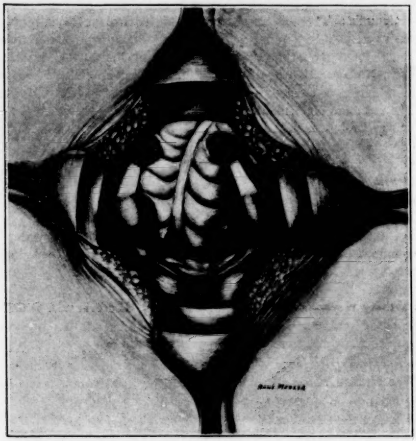

Fig. 3.—Our conception of the patient's pelvic anatomy. This composite drawing was made from a number of photographs none of which singly showed the entire operative field.

assured. Similarly, when a sperm containing a y-chromosome fuses with an x-chromosome of the ovum an individual bearing the characteristics of the male is to be expected.) It should be borne in mind that each fused cell or zygote is potentially bisexual, even though under normal conditions the characteristics of one sex are dominant while those of the other are submerged.

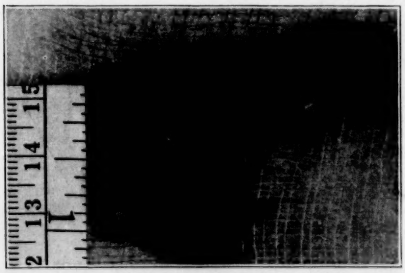

Fig. 4.—The specimen was excised from the right side of the pelvis. The portion that is pinned together is the rudimentary uterus. From it extend the gonad and the fallopian tube.

Why and how at one point of embryologic development a sudden change or switch in the character of the gonads occurs, followed by a subsequent maldevelopment of secondary sexual factors with endocrine rearrangement, cannot yet be answered. A true explanation is not forthcoming for this sudden twist of nature.

The following report was prompted by Novak's [2] record of an unusual instance of intersex. Owing to the fact that our case of intersexuality presents much in common with his, the case herein reported was carefully followed for three years and the report is submitted together with important operative and histologic observations. We agree with Novak that when such case presentations of intersexuality are prepared in the proper manner they can add much clarity to the befuddled status of the intersexes. Speculative reports on "evidences of hermaphroditism" based on imagination, presumption and "wishful thinking," such as were reported up until a few years ago, are not only unscientific but misleading.

REPORT OF CASE

History.—A housewife aged 29, of American descent, appeared before one of us on June 6, 1938 with a vague complaint of

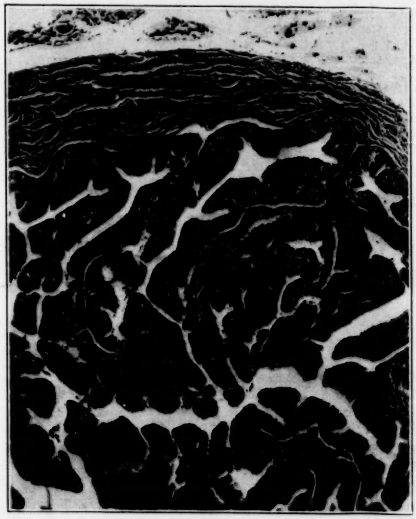

Fig. 5.—Section under low power magnification of the patient's normal fallopian tube.

abdominal pain. She also complained of headaches and dizziness. The fact that she had never menstruated did not seem to concern her much.

In her family history one interesting feature was the fact that her sister, two years younger than the patient, had also never experienced a menstrual period. A brother and two other sisters are married and have children.

The patient's infancy was normal and she experienced the routine childhood diseases as she approached adolescence. When she was 16 years of age she was examined by a local physician, vaginally and rectally, to ascertain the cause of her amenorrhea. Her family was told that the young girl was born somewhat different from other girls in that she did not possess a uterus. At about this time she commenced to suffer with backaches, abdominal cramps and headaches. She was still suffering with the abdominal cramps and headaches when first seen by us some thirteen years later. Her weight in adolescence had ranged between 95 to 100 pounds (43 to 45 Kg.). In the year

and Hermaphroditism, J. Urol. **42:** 1130, 1939. Moehlig, R. C., and Allen, N. M.: Intersexuality, J. A. M. A. **112:** 1938 (May 13) 1939. Kell, R. C.; Matthews, R. A., and Bockman, A. A.: True Hermaphroditism; Report of a Confirmed Case, Am. J. M. Sc. **197:** 825, 1939. Schiller, W.: Congenital and Acquired Sex Changes, Internat. Clin. **3:** 86 (Sept.) 1940 (contains an interesting review of the entire subject). Finkler, R. S.: Pseudohermaphroditism, Pregnandiol Glucuronidate Excretion, J. Clin. Endocrinol. **1:** 151, 1941.

2. Novak, Emil: Sex Determination, Sex Differentiation and Intersexuality, J. A. M. A. **105:** 413 (Aug. 10) 1935.

prior to our first seeing her she gained approximately 25 pounds (11.3 Kg.), making her weight about 125 pounds (56.7 Kg.) when she was first seen.

She had never had any sexual desire for the opposite sex and, although she had been married for eight years, she never experienced any sex urge toward her husband.

Fig. 6.—Section under low power magnification of gonad (testis) taken from patient, showing numerous interstitial cells.

She has few interests in life and does her own housework. She attends the movies occasionally and has a few women friends. She is quite attractive, has feminine charm and is of a very pleasant nature. She is neither bothered nor depressed about her amenorrhea; she would like to have children although she realizes that this is quite an impossibility. She dresses effeminately and with true girlish style. Her mentality is good.

Physical Examination.—General Appearance: The patient is white, of the Anglo-Saxon type, is 62½ inches (159 cm.) tall, weighs 124 pounds (56.2 Kg.) nude, and has normal and abundant blonde hair on her head and eyebrows but complete absence of axillary, pubic, perineal and anal hair. Her stature is slightly lordotic in the lumbosacral area of the spine, and her bony framework is light and thin. There is an excess of fat over the lower part of the abdomen and buttocks. The temperature, pulse rate and respiratory rate are normal.

Skin: Her skin is soft and pale, is covered with lanugo and has the soft tender touch similar to that of the skin of an infant. There are no acneiform lesions, lentigines, moles, warts or blemishes of any type. The skin about the vulva and rectum is scarcely pigmented and is of the same consistency as the rest of the skin. Her scalp is dry and the hair on her head is blonde and soft. When first seen, the breast areolas lacked pigmentation and the nipples were absent. The breasts were smaller than normal and the glandular consistency was abnormal.

Head and Neck: Her eyes are blue and the lashes are long. No abnormalities are noted except for two large central incisors in the upper set of teeth. Engelbach used this sign as being diagnostic of hypo-ovarianism.

Chest: Her bony thorax is small and delicate. The heart and lungs are essentially normal. The blood pressure is 90 systolic and 46 diastolic. Axillary hair and breast nipples are absent.

Abdomen: There is a layer of fat over the abdomen about 1½ inches in thickness. There are no scars, masses, tenderness, rigidity or pain on palpation. The abdominal aorta is easily palpable owing to an anterior curvature of the spinal column.

Extremities: The upper and lower extremities are fairly normal, although somewhat longer than usual.

Genitals: There is an absence of the normal pubic hair over the mons pubis. The labia majora and minora are smaller than usual. Although the clitoris is present and is normal in size, there is no erection of this organ on stimulation. There is also an absence of sexual excitation on palpation of the clitoris. The vestibule is normal and contains the openings of the urethra, vagina and accessory glands. There are no remnants of a hymen. The vagina, although its external opening is of normal size, is short in depth. On bimanual examination there is no cervix dipping into the vagina, nor is there a uterine body palpable. The ovaries and fallopian tubes are also not palpable. The posterior vaginal vault is so taut that it is difficult to feel much of anything through the vagina. A rectovaginal examination revealed no further information. Examination of the vagina with a speculum disclosed the similarity of the vaginal canal to a blind pouch. There is no cervix, os or anything resembling a cervix or os uteri. There is no opening into the abdominal cavity. The vaginal p_H, as determined with nitrazine paper, ranged between 4.5 and 5.

Laboratory Reports.—The basal metabolic rate was minus 4; Wassermann reaction, negative; complete blood count, normal; urine, normal; blood sugar, 71 mg. per hundred cubic centimeters of blood; blood nonprotein nitrogen, 32 mg. per hundred cubic centimeters of blood; vaginal p_H, between 4.5 and 5. Cellular study of vaginal washings did not seem abnormal; urinary estrogen and gonadotropic substance and blood estrogen and gonadotropic substance (serum) showed no increase over

Fig. 7.—Higher magnification showing immature seminiferous tubules in gonad of patient.

normal; a roentgenogram revealed no abnormalities; roentgen examination of the transabdominal pneumoperitoneum showed no signs of the presence of the uterus in the pelvis or abdomen.

Impressions.—At this time (before any therapy was started in 1938) the impressions gained were as follows: (1) primary

hypo-ovarianism, (2) congenital absence of uterus, (3) absence of breast nipples, (4) absence of axillary, pubic, perineal and anal hair.

At this time, the case was first reported in the literature as being illustrative of primary hypo-ovarianism with congenital absence of the uterus.[3] For a period of eighteen months following the first report she was carefully watched and studied. In order to stimulate her libido and to attempt to render her life more normal, she was given estrogenic substances[4] and later diethylstilbestrol.[5] These substances were hugely successful in increasing the size of her breasts and nipples and in stimulating a new sense of sexual desire not previously experienced.

All during this time she continued to complain of the vague pain in the lower part of the abdomen, which at times became more severe directly over McBurney's point. This manifestation was considered separate from her other disorders and was assumed to be due to a mild form of recurrent appendicitis. She was cautioned that if some day she should experience a severe attack of this pain her appendix would have to be

Fig. 8.—Ductus deferens-like structure which was closely associated with the testis.

removed and at the same time inspection of the pelvic organs would be undertaken.

On March 25, 1940, after all estrogenic therapy had been discontinued for about two months, she appeared at the office of one of us with a severe right-sided abdominal pain. The long-awaited opportunity for appendectomy and exploratory laparotomy was at hand. She was accordingly admitted to the Jewish Memorial Hospital, where she was soon operated on.

Operation (Gynecology Service of Dr. Edward Hoenig).—A right rectus incision was made and the appendix, which was hyperemic and inflamed, was located. It was excised by the clamp and cautery method. The pelvis was next explored and a most unusual peculiarity presented itself (fig. 1): The bladder was found but there was no uterus in relation to it. Instead, extending upward and laterally from the bladder on each side of the pelvis was a ligamentous cord, the upper end of which was attached to a small muscular organ about the size of a chestnut. These cords resembled bilateral rudimentary uteri. From each of these small bodies a thin fold extended to the lateral pelvic walls. These were probably vestigial broad ligaments. Within the broad ligaments and on each side was what appeared to be a fallopian tube in close association with each muscular body. Lying within the upper portion of each of the broad ligaments was a gonad. These gonads were similarly coated with a whitish capsule and were attached to the upper poles of the rudimentary uteri. There were no graafian follicles present in either gonad and the gonads seemed to be quite peculiar and atrophic. The uppermost ends of the broad ligaments were marked by clusters of small cystic nodules. The entire mass on the right side was removed for study. The other side was left intact, since we felt that total castration could do no good. Moreover, it was quite possible that even if a gonad appeared atrophic it might still have some endocrine function.[6] The department of pathology examined the specimen and its interesting and unusual observations are here reported.

Pathologic Examination.[7]—Gross: The specimen consisted of a V shaped mass measuring about 3 cm. in length in one axis and about 4 cm. in the other (fig. 2). The external surface was covered with a somewhat thickened and smooth serosa. A thin walled cyst, measuring about 0.5 cm. in diameter, was attached to one end of the specimen. On section through the smaller axis a whitish mass with somewhat fibrous structure could be seen. On section through the other extremity of the specimen the cut surface showed a rather thick, grayish white capsule and grayish red stroma. A rounded yellowish area measuring about 2 mm. in diameter was present in this portion of the specimen, the cut surface of which was smooth. Attached to the longer axis was a fallopian tube which showed externally and on section no gross pathologic condition.

Microscopic: Sections from the thick musculature of the organ suggested an atypical uterus, owing to the presence of intertwining, closely placed, rather hypertrophic bundles of smooth muscle with distinct simulation of the uterine wall. The included blood vessels showed sclerosis and thickening. No endometrium was included in the sections.

Section through the fallopian tube (fig. 3) showed folded mucosa with characteristic ciliated epithelium and muscle structure. In the wall was some aberrant glandular tissue with adjacent closely placed muscle tissue. One area showed a large cystic space with low cuboidal epithelium resembling a hydatid.

Section of a gonad showed typical undifferentiated immature testicle structure with considerable intervening fibrosis (fig. 4). The capsule corresponding to the tunica albuginea was thickened and showed some smooth muscle. The bulk of the tissue was occupied by seminiferous tubules without differentiation of lining epithelium (fig. 5). The cells showed columnar arrangement with orientation at the nuclei. In none of the tubules could any attempt at differentiation or spermatogenesis be seen. In the stroma, wide islands of interstitial cells were prominent. These cells contained considerable lipochrome. Sinusoidal areas with an erectile appearance were also present in the stroma of the gonad. No ovarian stroma was seen in any of the sections.

One of the sections close to the gonad showed tissue resembling ductus deferens structure (fig. 6) by close approximation of developed smooth muscle and central epithelial lining.

SUMMARY

A patient exhibiting unusual intersexuality had all the aspects of a female but her gonads were definitely abdominally retained immature testes, and there was complete absence of ovarian tissue. Sufficient numbers of complete reports of such cases, when carefully studied, may be capable of eventually explaining the etiology of such unnatural switches in nature.

3. Weisman, A. I.: Complete Absence of the Uterus, M. Rec. **150**: 392, 1939.

4. Weisman, A. I.: Breast Development from Estrogenic Hormones, with Report of a Case of Primary Hypo-Ovarianism, M. Rec. **151**:391, 1940.

5. Weisman, A. I.: Rapid Breast Changes from Stilbestrol, Clin. Med. & Surg. **48**: 146, 1941.

6. Despite the fact that one gonad was left intact, the patient has since commenced to suffer with severe hot flushes that are typical of the menopause. Repeated and large doses of estrogenic therapy have been necessary to control these attacks since the operation.

7. From the laboratory of Dr. Alfred Angrist.

PROGRESSIVE SUBCORTICAL ENCEPHALOPATHY

(ENCEPHALITIS PERIAXIALIS DIFFUSA; SCHILDER'S DISEASE)

JOHN J. O'DONNELL, M.D., ERIE, PA.

The following conditions are rarely if ever found in combination, namely a rare disease, a fairly exact measurement of intelligence before and after the onset of the disease and the confirmation of diagnosis at autopsy. All these conditions are present in the case herewith reported.

REPORT BY SCHOOL PSYCHOLOGIST

Zoe I. Hirt, school psychologist of the child study department, Erie, Pa., contributed the following history, obtained from the mother of the patient, E. S.:

The father was an alcoholic. The mother had pneumonia when seven months pregnant. She was threatened with an abortion and spent two weeks in bed. The child was born at full time, a blue baby. He had respiratory difficulties until his tonsils and adenoids were removed at the age of 3 years. At the age of 4 years he had infected ears and was treated in the hospital for two weeks. At 6 he fell from a garage roof and broke one of his arms just below the shoulder. His mother expressed the belief that his head was injured by the fall. A year later he was struck on the head by a horseshoe. The blow left a deep cut which was slow to heal. In the spring of 1939 he had severe ivy poisoning.

In November 1938 when the boy took the Kuhlmann-Anderson group intelligence tests with his fifth grade class he ranked second among 26 pupils, his intelligence quotient on that scale being 107. His conduct in school was excellent and his personal appearance good.

On June 11, 1940 the assistant principal of East High School sent him in for a psychologic examination because of his undesirable conduct. The complaints were frequent truancies, stubborn refusal to participate in class activities and recitations, failure to prepare and hand in assignments for out of class study, unwillingness to take part in classroom activities, disorderly conduct in the school corridors, remaining away from home until late at night, wandering aimlessly around the streets, destructiveness at home and outside, untidiness at meals, pushing his food from his plate and extreme restlessness.

On examination the boy was neat in appearance but had a shuffling gait and was restless, shifting his position continually from the back of his chair to the edge of the seat and rubbing and scratching his arms and wrists. Every little while he would hold the index finger of his right hand in front of his mouth and blow against it. His speech was thick, and at times he stuttered. Verbal responses were slow. Questions had to be repeated, sometimes over and over. When asked to explain his undesirable conduct in school he said "I want to fail; I can't do seventh grade work; it's too hard."

Form L of the 1937 revision of the Stanford-Binet scale was used to investigate his mental equipment on June 11. He succeeded with all the tasks at year 7 and above that level with additional items scattered thinly as far as year 12. He lacked barely one month of being 13, and his only successes at the 12 year level were in two vocabulary items. He could not retain more than five digits for immediate recall after he heard them. He could not read a word of the little paragraph printed under year 10 on the test scale. It was obvious that he could not see the words, so a first reader selection in large type was placed before him. After much effort, holding the page close to his eyes, he read "A boy ran along" instead of "A boy had a dog." He could not keep his place on the page as he continued to read the little selection. He said that he should receive a nickel in change if he gave a storekeeper 15 cents in payment for a 12 cent article. He thought that his change should be 14 cents from a quarter if he bought something costing 4 cents. He repeated the same five or six words over and over when asked to name all the different words he could think of in a minute. He seemed totally lacking in critical judgment. The sum of his correct responses in the test gave him an intelligence quotient of 63.

HOSPITAL REPORT

E. S. was admitted to Hamot Hospital Oct. 13, 1939 with cellulitis of the floor of the mouth. He had had an upper molar on the right side extracted five days before. The day after extraction he began to have swelling on the under surface of the mandible on the right side. The swelling gradually became enlarged and though not inflamed was extremely tender to touch. The next day he began to have chills and weakness. His mother applied ice bags to his jaw and forced fluids. The chills had persisted, but the swelling on the jaw had not altered much since three days before admission.

The Wassermann and Kline reactions of the blood were negative and the blood counts normal. The temperature on admission was 102.2 F., but it rapidly subsided under treatment with 15 grains (0.9 Gm.) of sulfanilamide and 10 grains (0.6 Gm.) of sodium bicarbonate every four hours.

The patient was discharged as cured on October 23.

On June 12, 1940 he came to the neuropsychiatric clinic, and he was admitted to the ward for study. He had an unsteady gait, failing vision and a dull mentality.

On physical examination he appeared well developed and nourished. Neurologic examination revealed that the pupils were regular, dilated and reactive to light and in accommodation. The visual acuity admitted by the patient was 20/100 in each eye. Tests of refraction revealed that there was small hyperopic astigmatic correction, and on prodding the examiner could get the patient to read with a 20/50 acuity in each eye. Fundus examination gave normal results throughout. There was very pronounced concentric contraction of the visual fields but no significance in the boy's responses. Examination of the eyes revealed nothing of definite significance from the diagnostic standpoint.

The speech was slow. There was no restriction of the tongue or the palate and no stiffness of the neck. The tendon reflexes were increased. The epicritic and deep sensibility was increased. There was no Babinski, Gordon, Oppenheim or Chaddock reflex, but Romberg's sign was present. The gait was spastic. There were incoordination of the arms and legs and past pointing. The abdominal and cremasteric reflexes were normal. Kernig's sign was not present. The vibratory sense was normal. The patient was unable to do the heel to shin and toe to finger tests.

On examination of the spinal fluid the pressure was 6 and the cell count 4. There was a slight increase in the globulin content. The Wassermann reaction was negative. The blood showed a hemoglobin content of 86 per cent, 6,700 leukocytes and 5,320,000 erythrocytes. The color index was 0.8. The Wassermann and Kline reactions of the blood were negative.

Roentgen examination revealed that the bones of the skull were of normal density and thickness. No abnormal shadows were seen, and there was no evidence of increased intracranial pressure. The sella turcica was small and of the enclosed type. Nothing was seen to indicate pressure or change in the bone in this region. The sphenoid sinus was large.

With the foregoing data, tumor of the brain could be ruled out with some degree of certainty. The mental deterioration, failing vision and spastic gait being taken into consideration, a diagnosis of progressive subcortical encephalopathy (Schilder's disease, or encephalitis periaxialis diffusa) was made. The boy was sent home June 17.

During the interval between the patient's discharge and readmission to the hospital I saw him at home once a week. The vision became progressively worse, and there was more dulling of intelligence.

He was sent into the hospital on August 4. On admission he was apparently unconscious, the neck was rigid and retracted

The laboratory studies and autopsy were done by Dr. E. L. Armstrong, the ophthalmic examination by Dr. James Delaney and the roentgen examination by Dr. B. Swayne Putts.

and the whole body would jerk most of the time. The eyes were open but sightless. The boy would cry from pain.

At this time the deep tendon reflexes were lost. Kernig, Babinski, Gordon, Oppenheim and Chaddock reflexes were present bilaterally. Opisthotonos was present at times and incontinence of the bowels and the bladder. Stertorous respiration was constant. Only a small amount of fluid was taken. The patient was unable to swallow solids. The temperature was between 99 and 104 F., and he was in a stupor at all times.

The only medication given was morphine to relieve pain. Death occurred on August 19.

AUTOPSY REPORT

External Examination.—The body was emaciated. The height was 63 inches (160 cm.) and the weight approximately 80 pounds (36.3 Kg.). The superficial layers of the skin of the trunk were raised in tiny blebs that brushed off easily when the skin was rubbed. These blebs were filled with clear watery fluid. No edema or jaundice was noted and no enlargement of the superficial lymph nodes. No scars or marks of injury were seen on the body surface. The joints throughout the body appeared fixed, apparently from prolonged muscle spasm.

Eyes: The pupils were unequal but regular, and both were dilated. The left pupil was 7 mm. and the right 8 mm. in diameter.

Internal Examination.—Brain: On removal of the skull cap the vessels of the meninges were seen to be everywhere injected. No gross hemorrhage was present and no free exudate was seen over the surface of the brain. On serial section the white matter throughout the brain showed dilated vessels and apparently minute areas of hemorrhage. No gross degeneration or abscess formation was noted.

The dura was stripped from the base of the skull and the sinuses and middle ears examined. The mastoid cells and the middle ear on the left side were filled with a yellowish mucopurulent secretion. The right middle ear and mastoid cells were dry, as were the bony sinuses.

Thorax: On removal of the chest wall both lungs lay free. There was no free fluid in the pleural cavities. The lungs were crepitant throughout and showed no evidence of consolidation. No hemorrhage was noted beneath the pleura.

Heart: The amount of pericardial fluid was not increased. Examination of the myocardium and the heart valves revealed nothing remarkable.

Abdomen and Pelvis: Gross examination of the organs in the abdomen and the pelvis revealed nothing definitely pathologic.

Bacterial Flora: Smears of material from the left mastoid cells showed many staphylococci and numerous short chain streptococci. Cultures of material from the brain surface were sterile, as were cultures of the blood.

Microscopic Examination of Brain.—Fourteen blocks were taken from different areas in the cerebral and cerebellar cortex. In examination of these sections the following microscopic changes produced by progressive subcortical encephalopathy were noted:

1. The myelin sheaths of the white matter were destroyed and in places disintegrated. This was particularly noticeable in the sections of cerebral cortex and at a few points was noted to extend into the margins of the gray matter. Multiple foci were observed.

2. The perivascular spaces were greatly enlarged from retraction of the surrounding neuroglial tissue.

3. There were diffuse perivascular accumulations of lymphocytes, with scattered plasma cells. In some sections this perivascular infiltration was dense and was seen not only in the vessels lying deep in the white matter but in the meninges.

The anatomic diagnoses were (1) hyperemia and engorgement of the meningeal vessels and (2) the presence of free pus in the left mastoid cells and the left middle ear. The cause of death was progressive subcortical encephalopathy.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING STATEMENT.

THEODORE G. KLUMPP, M.D., Secretary.

HALOGENATED VEGETABLE OILS FOR BRONCHOGRAPHY AND THE PROBLEM OF LIPID PNEUMONIA

The manufacturer of a preparation of iodine and chlorine in peanut oil for intratracheal administration as a bronchographic medium has recently called attention to the following statement occurring in the editorial "Lung Irritation Following the Use of Certain Oil Preparations" (THE JOURNAL, April 26, 1941, p. 1911): "Several of the vegetable oils, notably croton oil, castor oil and peanut oil, are exceedingly active irritants of tissues." The manufacturer points out that this statement has led to inquiries from physicians which indicate that members of the medical profession do not understand that this statement does not apply to refined grades of peanut oil from which irritating unsaturated fatty acids have been eliminated, such as the completely saturated halogenated product which it manufactures.

The editorial containing the statement in question was based on a previous report by Dr. Paul R. Cannon (The Problem of Lipid Pneumonia, THE JOURNAL, Dec. 21, 1940, p. 2176), published under the auspices of the Council on Pharmacy and Chemistry, which deals primarily with the promiscuous intranasal use of oily inhalants, particularly those containing liquid petrolatum. Regarding the manufacturer's point that saturated peanut oil is not as irritating as the crude unsaturated oil, Dr. Cannon explains that, while it appears reasonable that complete saturation with removal of free fatty acids should eliminate some of the irritating properties of this and other vegetable oils, the problem has not been adequately studied. He emphasizes, however, that this problem should not be confused with that of lipid pneumonia resulting from the constant use of nasal oil drops, since, even if slightly irritating, halogenated oils for bronchographic study are used relatively infrequently and then only under the supervision of a roentgenologist.

The Council concurs with the view expressed by Dr. Cannon that the problem of lung irritation from the use of oils other than petrolatum needs further study, especially from the standpoint of inhalant preparations which are subject to unsupervised use by the public.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

THEODORE G. KLUMPP, M.D., Secretary.

EPINEPHRINE (See New and Nonofficial Remedies, 1941, p. 251).

SOLUTION OF EPINEPHRINE HYDROCHLORIDE 1:1,000-LAKESIDE.—A brand of solution epinephrine hydrochloride-U. S. P. containing chlorobutanol 0.5 per cent and sodium bisulfite 0.1 per cent in physiological solution of sodium chloride, saturated with carbon dioxide.

Manufactured by The Lakeside Laboratories, Inc., Milwaukee.
Solution of Epinephrine Hydrochloride 1:1,000-Lakeside, 1 cc. ampule.
Solution of Epinephrine Hydrochloride 1:1,000-Lakeside, 30 cc. rubber stoppered vial for parenteral administration.

McKESSON'S NATURAL VITAMINS A AND D IN OIL, 6 CC.—A concentrate of vitamins A and D prepared from medicinal cod liver oil, the concentrate containing not less than 60,000 U. S. P. units of vitamin A and not less than 10,000 U. S. P. units of vitamin D per gram.

Actions and Uses.—It possesses the therapeutic properties recognized for the vitamins present in cod liver oil.

Dosage.—Six drops per day. Larger dose as prescribed by the physician.

Manufactured by the International Vitamin Corporation, New York. (McKesson & Robbins, Inc., Bridgeport, Conn., distributor.) The vitamin D concentrate used is made under U. S. patent No. 1,690,091 (Oct. 30, 1928; expires 1945).

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 27, 1941

A CALL TO THE MEDICAL PROFESSION

The nation is at war. The Congress has passed an amendment to the Selective Service Act which will call for registration of every man up to the age of 65 and which will place all men under 45 years of age subject to service at the order of the Selective Service boards.

The Procurement and Assignment Service for Physicians, Dentists and Veterinarians was established by order of the President on October 30. Thus the medical profession itself aids in determining proper distribution of the medical profession in supplying the needs of the armed forces and maintaining medical service to civilian communities, public health agencies, industrial plants and other important needs.

At a meeting of the Procurement and Assignment Service held in Chicago at the headquarters of the American Medical Association on December 18 jointly with the Committees on Medical Preparedness of the American Medical Association, the American Dental Association and the American Veterinary Medical Association, plans were drawn for making immediately available to the United States Army and Navy Medical Corps the names of physicians who wish to be enrolled promptly in the service of the government in this emergency.

On the opposite page is published a blank by which every physician may at once place his name with the Procurement and Assignment Service as one who is ready to serve the nation as the need arises. If you wish to make yourself available for classification, fill out this blank and send it at once to Dr. Sam F. Seeley, Executive Director of the Procurement and Assignment Service. When these blanks are received, they will be classified and checked with the information available in the national roster of physicians at the headquarters of the American Medical Association.

For two thousand and nine counties in the United States, lists have been prepared indicating physicians who are engaged in necessary civilian projects, public health services or educational activities from which they cannot be spared. Shortly the rest of the counties will have such lists available.

In each of the corps areas covering the United States a committee is being established, including representatives of medical, hospital, educational, dental and veterinary activities. In the individual states, committees of medical, dental and veterinarian professions are being established through which the corps area committees will exercise their functions. In each county also local committees will provide accurate information regarding the status of each member of the profession concerned.

The raising of the Selective Service age from 28 to 45 will place a great number of additional physicians in the category of those on whom the nation may call as their services are needed. Estimates indicate that some sixty thousand physicians thus become available for service and that forty-two thousand dentists under the age of 45 also become subject to call. By enrolling with the Procurement and Assignment Service immediately, utilizing the blank on the opposite page, all physicians, but particularly those under 45 years of age, insure to every extent possible assignment to the type of service for which they are best fitted. They avoid thus also the possibility of unclassified service with the United States Army during the period that may be necessary following selection by the Selective Service before the commission can be secured. A physician called by the Selective Service who has not enrolled or who is not on a reserve list obviously serves without a commission during the time that necessarily elapses before a commission is secured. In future issues of THE JOURNAL announcements will be made regularly of the numbers of those who enroll and of the extent to which the immediate needs of the Army, Navy and other government agencies are being supplied.

ENROLMENT FORM FOR PROCUREMENT AND
ASSIGNMENT SERVICE FOR PHYSICIANS

Dr. Sam F. Seeley, Executive Officer
Procurement and Assignment Service
New Social Security Building
4th and C Streets S.W.
Washington, D. C.

Dear Doctor Seeley:

Please enroll my name as a physician ready to give service in the Army or Navy of the United States when needed in the current emergency. I will apply to the Corps Area commander in my area when notified by your office of the desirability of such application.

Signed _____

1. Give your name in full, including your full middle name:

2. The date of your birth:

3. The place of your birth:

4. Are you married or single?

5. Have you any children? If so, how many?

6. Do you believe yourself to be physically fit and able to meet the physical standards for the Army and Navy Medical Corps?

7. Have you filled out previously the questionnaire sent to all physicians by the American Medical Association?

8. When and where were you graduated in medicine?

9. In what state are you licensed to practice?

10. Do you now hold any position which might be considered essential to the maintenance of the civilian medical needs of your community? If so, state these appointments:

11. Have you previously applied for entry into the Army or Navy Medical Service? If so, state when, where and with what result (if rejected, state why).

Signature _____

Date _____ Address _____

Fill out this blank, tear out and send to Dr. Sam F. Seeley at the above address.

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9. In what state are you licensed to practice?

10. Do you now hold any position which might be considered essential to the maintenance of the civilian medical needs of your community? If so, state these appointments:

11. Have you previously applied for entry into the Army or Navy Medical Service? If so, state when, where and with what result (if rejected, state why).

Signature _____

Date _____ Address _____

Fill out this blank, tear out and send to Dr. Sam F. Seeley at the above address.

CONGRESS ACTS TO SAFEGUARD USERS OF INSULIN

Congressional action on legislation to protect the users of insulin was completed on December 19. Prompt action was necessary because the patent on insulin, held by the University of Toronto, under which patent adequate standards of purity and strength have been maintained, expired on December 23.

The legislation that has been enacted amends the Federal Food, Drug and Cosmetic Act by declaring a drug to be misbranded if it is, or purports to be, or is represented as a drug composed wholly or partly of insulin unless (1) it is from a batch with respect to which a certificate or release has been issued under regulations to be promulgated by the Federal Security Administrator and (2) such certificates or release is in effect with respect to such drug. The Federal Security Administrator is directed to provide for the certification of batches of drugs composed wholly or partly of insulin. A batch of any such drug, the legislation provides, shall be certified if the drug has such characteristics of identity and such batch has such characteristics of strength, quality and purity as the Administrator prescribes in such regulations as necessary adequately to insure safety and efficacy of use. Prior to the effective date of such regulations, the Administrator is authorized, in lieu of certification, to issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Regulations providing for such certification must, among other things, contain provisions prescribing (1) standards of identity and of strength, quality and purity, (2) tests and methods of assay to determine compliance with such standards, (3) effective periods for certificates and other conditions under which they shall cease to be effective as to certified batches and as to portions thereof. The regulations, the legislation provides, shall prescribe no standard of identity or of strength, quality or purity for any drug different from the standard of identity, strength, quality or purity set forth for such drug in an official compendium such as the United States Pharmacopeia or similar publication. The Pharmacopeia has adopted standards for insulin.

In explaining the purpose of the legislation and the urgency of the need for immediate action, Representative Lea of California made this statement on the floor of the House of Representatives:

> There is an emergency situation that caused our committee to act on this bill at the present time. The report before the House represents the unanimous opinion of the committee.
>
> The patent on insulin expires on the 23d of this month. Control of the manufacture of insulin is in the hands of the University of Toronto. The patent is owned by the University of Toronto, and manufacturers in the United States act under license from the committee on insulin of that university.
>
> Control of insulin quality by the University of Toronto has been most commendable. That control has been on a nonprofit, humane and scientific basis. It has required that all manufacturers comply with the standards set up by the committee on insulin in order to engage in its manufacture or sale. This control was through ownership of the patent right.
>
> On expiration of the patent, present control over the situation will cease and manufacturers in this country would be at liberty to manufacture and place insulin on the market in disregard of that uniform standard of quality and strength that are so essential for the protection of users of insulin.
>
> Over one million people in the United States are now under insulin treatment. It is estimated they are spending about $15,000,000 a year for this remedy. Ordinarily the doctor gives the patient a prescription, who after that buys from any drug store available. So far the afflicted person has had the protection that is given by a uniform standard and strength under the restrictions imposed by the owners of the patent.
>
> The effect of insulin is such that injury and death may result from taking too much or too little. The peril to the public that would ensue from the lack of a uniform standard would be primarily due to the variation and uncertain quality as to strength and purity unless its standardization is assured by the federal government acting through the Food and Drug Administration.
>
> Under the amendment here proposed to the Food, Drug and Cosmetic Act, every batch of insulin would be submitted to tests to assure its freedom from infection, its purity and strength. Each batch would be subject to approval of the Food and Drug Administration and rejected if not of a properly standardized quality. By this means all users of insulin suffering from diabetes can be assured of the quality, the standard, strength and purity of their purchases.
>
> The procedure required in making tests, the adoption of regulations to control such tests and the certification thereof by the Food and Drug Administration will conform to the practice that already prevails in requiring such tests, and issuing such certificates as to certain coal tar products.

THE FORMATION OF URINE

The early studies of Bowman, who maintained that the glomeruli of the kidney acted as filters and the cells of the tubules as secreting agents, together with the work of Heidenhain, who championed the conception that the formation of urine was entirely a secretory process, and the ideas of Ludwig, who thought that a process of absorption might occur in the tubules of the kidney, contribute interesting early chapters in the story of renal function. The more modern view so well expressed by Cushny,[1] according to which the excretion of urine involves simple filtration in the glomeruli coupled with selective reabsorption in the tubules, is now familiar. The classic work of Wearn and Richards,[2] who some two decades ago collected glomerular urine directly from Bowman's capsule in the living frog kidney by means of a capillary pipet, opened a new route of attack on the problem of glomerular and tubular function. Since that time methods have been developed for the collection of fluid from single tubules of the amphibian kidney, and the analysis of the minute amounts of fluid collected has been accomplished. The results of these studies has lent powerful support to the filtration-reabsorption theory of urine formation.

The mammalian kidney has now been successfully used in this type of study. In recent reports, Walker

1. Cushny, A. R.: The Secretion of the Urine, ed. 2, New York, Longmans, Green & Co., Ltd., 1926.
2. Wearn, J. T., and Richards, A. N.: Observations on the Composition of Glomerular Urine, with Particular Reference to the Problem of Reabsorption in the Renal Tubules, Am. J. Physiol. **71**: 209 (Dec.) 1924.

and his co-workers [3] describe their interesting experiments on the kidneys of anesthetized animals, particularly rats and guinea pigs. These investigators were able to collect amounts of fluid sufficient for quantitative microanalysis from a single glomerulus, proximal tubule and distal tubule. By a procedure involving microdissection of the nephrons, the precise site of the collection could be identified. Unfortunately, only in guinea pigs could glomeruli be found which were accessible for study. Certain portions of the proximal and distal tubules in guinea pigs, rats and other mammals are conveniently located with regard to the possibility of collecting fluid from them. Analyses of glomerular fluid reflect the filtering function of the glomerulus. While little or no protein was found in the glomerular filtrate, it did contain reducing substances and creatinine in concentrations similar to those existing in blood plasma. The reducing substances are reabsorbed as fluid flows through the proximal tubule. The site of dextrose absorption is therefore the same in the mammalian and the amphibian kidney. At least two thirds of the fluid also appears to be resorbed within the proximal tubule. As pointed out by Walker and his co-workers, this is the reverse of the situation demonstrated in amphibians and it supports the suggestion of Smith that "in the mammal a great part of the water might be reabsorbed in the proximal tubule." [4] While fluid reabsorption in the mammalian tubule is accomplished without any increase in the osmotic pressure of the fluid remaining within the tubule, it is not by any means a purely passive reabsorption of unchanged glomerular filtrate. Proximal tubular fluid possesses a distinctly higher percentage of chloride than does plasma. The ratio of the chloride concentration in the former fluid to that in plasma appears to reach an average of 1.4 in the first third of the proximal tubule and to remain at that point without further increase throughout the second third of this segment. These observations are apparently indicative of preferential reabsorption of another ion, presumably bicarbonate, in the proximal tubule. On the other hand, since most of the bladder urine specimens in the experiments were found to be hypotonic to plasma with respect to chloride, some further portion of the nephron must reverse the concentration ratio of the proximal segment and preferentially reabsorb the chloride ion.

The recent work of Walker and his associates on the collection and quantitative analysis of glomerular and tubular fluid from mammalian kidneys forms a logical extension of the work initiated by Richards and his co-workers on amphibians. The continued prosecution of these studies will serve further to elucidate problems associated with renal function.

3. Walker, A. M., and Oliver, J.: Methods for the Collection of Fluid from Single Glomeruli and Tubules of the Mammalian Kidney, Am. J. Physiol. **134**: 562 (Oct.) 1941. Walker, A. M.; Bott, P. A.; Oliver, J., and MacDowell, M. C.: The Collection and Analysis of Fluid from Single Nephrons of the Mammalian Kidney, ibid. **134**: 580 (Oct.) 1941.

4. Smith, H. W.: The Physiology of the Kidney, New York, Oxford University Press, 1937. p. 232.

Current Comment

HEALTH ACHIEVEMENTS IN WISCONSIN

Various state medical societies have been undertaking the education of the lay public in health from different approaches. In previous issues of THE JOURNAL reference has been made to the program of the California Medical Association [1] and the programs of the medical societies of New York [1] and Georgia.[2] In Wisconsin the approach has been emphasis on the health achievements within the state. The Wisconsin State Board of Health has long been advertising Wisconsin as the third healthiest state in the United States on the basis of ratings by the National Resources Board. The state medical society has made this rating the keynote of a pamphlet [3] prepared with the cooperation of the state board of health and the state industrial commission. In this pamphlet, illustrated with pictorial statistics, photographs, vignettes and montages, are set forth health achievements in the state such as favorable rates of time lost from industrial jobs, addition of nineteen years to the average life expectancy at birth, over 99 per cent of babies delivered by physicians, low infant and maternal death rates, decline of communicable diseases, availability of hospital facilities, virtual conquest of typhoid, inspections of barber shops, beauty parlors, tourist cabin and summer resort inspections, and industrial and community sanitation. Medical education, postgraduate education and nursing education are dealt with in another section, as is registration of births and deaths. The third section of the booklet deals with unsolved problems in communicable disease control, accident prevention, community and industrial sanitation, heart, cancer, cerebral hemorrhage and nephritis. Emphasis is placed on the availability of physicians, who are at least as easily available as other necessary community facilities, except in three areas all of which are so sparsely populated that no physician could make a living there and even subsidies from local funds are but "a theoretical solution." The pamphlet closes with brief descriptions of eleven cooperative projects of the State Medical Society of Wisconsin with state and public agencies. Going a step further, a film strip has been developed consisting of one hundred frames, which sets forth the same general facts as those in the brochure and under the same title. Accompanying this film strip is an outline for an accompanying lecture.[4] This film strip is to be made available throughout the state for presentation by county medical societies or under their auspices to lay audiences. More and more the diversity of approach to lay health education by medical societies in various states and counties demonstrates original methods and emphasizes again the importance of free and uninhibited enterprise in an independent medical profession.

1. Doctors on the Air, Current Comment, J. A. M. A. **116**: 1648 (April 12) 1941.

2. State Society Purchases Sound Movie Equipment, Current Comment, J. A. M. A. **117**: 39 (July 5) 1941.

3. Health Achievements in Wisconsin, prepared by State Medical Society of Wisconsin, Madison, 1941.

4. Health Achievements in Wisconsin, prepared by Committee on Health and Public Instruction, State Medical Society of Wisconsin, Madison.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS, VETERINARIANS

At a meeting in Chicago of the board of the Procurement and Assignment Service with the Committees on Medical Preparedness of the American Medical Association, the American Dental Association and the American Veterinary Medical Association, a definite organization was completed for the functioning of this service in relationship to needs of professional personnel in the war.

PHYSICAL REQUIREMENTS FOR PHYSICIANS IN SERVICE

The Procurement and Assignment Service will make available shortly through publication in the periodicals of the professions concerned a tabulation of the physical requirements for physicians applying to any of the federal services.

EVALUATION OF PHYSICIANS THROUGH COUNTY MEDICAL SOCIETIES

More than two thousand county medical societies have already made available ratings of physicians available in such counties as regards their employment in essential services and their availability for the Army and Navy Medical services. Steps will be taken to speed up the completion of similar evaluations in the remaining counties.

QUESTIONNAIRE

Approval was given to the immediate publication in the professional periodicals of a questionnaire addressed to all members of the medical profession urging them to enroll at once with the Procurement and Assignment Service so as to make available immediately a pool of physicians from whom applicants for commissions might be drawn promptly. The immediate needs of the Army are for men in the grades of lieutenant and captain—that is to say, men particularly under the age of 45.

THE NATIONAL ROSTER

A conference was held with representatives of the National Roster, which is a subsidiary of the National Resources Planning Board. Arrangements were made for joint action with the Budget Committee in Washington to secure the necessary funds for operation of the National Roster covering the medical profession and for the regional office in the headquarters of the American Medical Association.

CORPS AREAS

Dr. James E. Paullin described the methods by which evaluation has been made of all men in the Fourth Corps Area and also the method by which ratings have been given to specialists.

Approval was given to the constitution of committees in each of the corps areas and associated naval districts to function as advisory to the corps area commander, the committee to consist of a chairman who will be the corps area representative of the Committee on Medical Preparedness of the American Medical Association, one physician representing medical education, one representing the hospital organizations, two physicians selected at large, two dentists and one representative of the veterinary profession. The chairmen nominated for the various corps areas are as follows:

First—Dr. W. G. Phippen, Salem, Mass.
Second—Dr. A. W. Booth, Elmira, N. Y.
Third—Dr. A. M. Shipley, Baltimore.
Fourth—Dr. Edgar Greene, Atlanta, Ga.
Fifth—Dr. E. L. Henderson, Louisville, Ky.
Sixth—Dr. Charles H. Phifer, Chicago.
Seventh—Dr. Roy W. Fouts, Omaha.
Eighth—Dr. Sam E. Thompson, Kerrville, Texas.
Ninth—Dr. Charles A. Dukes, Oakland, Calif.

Other physicians nominated to these corps area boards include:

First—Dr. Deering G. Smith, Nashua, N. H.; Dr. Lucius Kingman, Providence, R. I.
Second—Dr. S. J. Kopetzky, New York; Dr. W. J. Carrington, Atlantic City, N. J.
Third—Dr. C. H. Henninger, Pittsburgh; Dr. Hugh H. Trout, Roanoke, Va.
Fourth—Dr. Alfred A. Walker, Birmingham, Ala.; Dr. Edward H. Jelks, Jacksonville, Fla.
Fifth—Dr. Robert Conard, Wilmington, Ohio; Dr. Larue Carter, Indianapolis.
Sixth—Dr. J. Milton Robb, Detroit; Dr. Stephen E. Gavin, Fond du Lac, Wis.
Seventh—Dr. F. L. Loveland, Topeka, Kan.; Dr. Robert L. Parker, Des Moines, Iowa.
Eighth—Dr. Holman Taylor, Fort Worth, Texas; Dr. John W. Amesse, Denver.
Ninth—Dr. John Fitzgibbon, Portland, Ore.; Dr. John H. O'Shea, Spokane, Wash.

A regional office is to be established in each corps area for the maintenance of information, for supervision of the state committees and to act as a consulting body on all matters relating to the functions of the Procurement and Assignment Service in the corps area. The following dentists were recommended for appointment:

First—Dr. Philip Adams, Boston; Dr. Frank W. Rounds, Boston.
Second—Dr. William McG. Burns, Brooklyn; Dr. Allan T. Newman, New York.
Third—Dr. Lucian Brun, Baltimore; Dr. Harry Bear, Richmond, Va.
Fourth—Dr. Claude R. Wood, Knoxville, Tenn.; Dr. Ralph R. Byrnes, Atlanta, Ga.
Fifth—Dr. Earl Lowery, Columbus, Ohio; Dr. Wendell Postle, Columbus, Ohio.
Sixth—Dr. Leo Kremer, Chicago; Dr. Paul H. Jeserich, Ann Arbor Mich.
Seventh—Dr. F. A. Pierson, Omaha; Dr. A. W. Bryan, Iowa City.
Eighth—Dr. H. G. Duckworth, San Antonio, Texas; Dr. Fred C. Elliott, Houston, Texas.

Ninth—DR. B. C. KINGSBURY, San Francisco; DR. E. G. SLOMAN, San Francisco.

The following veterinarians were recommended for appointment:

First—DR. R. W. SMITH, Concord, N. H.
Second—DR. R. R. BIRCH, Ithaca, N. Y.
Third—DR. MARK WELSH, College Park, Md.
Fourth—DR. B. T. SIMMS, Auburn, Ala.
Fifth—DR. A. F. SCHALK, Columbus, Ohio.
Sixth—DR. WARD GILTNER, East Lansing, Mich.
Seventh—DR. H. D. BERGMAN, Ames, Iowa.
Eighth—DR. M. B. STARNES, Dallas, Texas.
Ninth—DR. C. M. HARING, Berkeley, Calif.

The names of the physicians representing medical education and those of the hospital organizations will be published later.

The technic was also described for supplying the names of physicians to appropriate governmental agencies according to the present methods of functioning of the Procurement and Assignment Service.

UNITED STATES CIVIL SERVICE COMMISSION NEEDS PHYSICIANS

The United States Civil Service Commission has issued a table showing the number of medical officers (Associate grade $3,200 per annum) needed in the immediate future in federal agencies. The positions are those in the civil service, for which the Civil Service Commission has the responsibility of recruiting, rating and maintaining registers of qualified eligibles. The needs are, of course, expected to vary as vacancies are filled or new positions are open. Later statements may be required as changes occur (see civil service announcement No. 130 of 1941). The table shows the following needs:

Veterans' Administration		
Optional Branches:		
Tuberculosis	2	
Neuropsychiatry	40	
General medicine and surgery	40	
Ear, eye, nose and throat	5	
Roentgenology	3	
Pathology	4	
Urology	2	
Orthopedics	2	
Cardiology	1	
Chest	1	
		100
U. S. Public Health Service		
Optional Branches:		
General practice	37	
Public health (general) or general practice	35	
		72
Indian Service		
General practice	32	
		32
Panama Canal Service		
General practice	15	
Eye, ear, nose and throat	1	
Pathology	1	
		17
Total		219
* U. S. Children's Bureau	10	

* Estimated need for calendar year 1942. Salary ranges $3,200 to $5,600 per annum. See civil service announcement No. 139 of 1941.

Requirements are:

Education.—Applicants for the Associate grade must have been graduated from a medical school of recognized (class A) standing with the degree of M.D. subsequent to May 1, 1930.

In determining the date of graduation of those physicians who have graduated from one of the medical schools which requires a one-year internship following the medical curriculum before conferring the degree of M.D., the commission, for the purpose of this examination, will consider as the date of graduation the time when the fourth year curriculum was successfully completed and not the date following the internship.

The applications of graduates from foreign medical schools whose graduates are admitted to the examination of the National Board of Medical Examiners will be accepted.

Experience.—Subsequent to graduation, applicants must have had one year of internship, general rotating or in a special branch.

Age Limit.—Applicants must not have passed their fifty-third birthday on the date of receipt of application. The age limit does not apply to persons granted military preference because of military or naval service except that such applicants must not have reached the retirement age.

Physical Ability.—Applicants must be in sound physical health. Remediable defects or curable disease will not exclude a person from examination, but proof that such defects have been remedied or the disease, if any, cured must be received during the life of the eligible register before persons otherwise qualified may be considered for appointment under civil service rules.

Vision must be at least 20/30 (Snellen) in one eye, glasses permitted. The applications of persons who have uncorrected vision of less than 20/200 (Snellen) in that eye, corrected to meet the foregoing requirement, will be suspended and they will not be eligible for appointment until satisfactory evidence has been presented to the commission showing that there is no disease or defect of the eye other than an error of refraction.

Ordinary conversation must be heard at a distance of at least 15 feet with one ear.

For some of these positions, applicants must be at least 5 feet 4 inches in height. The height requirement will be waived for veterans. Vision without glasses must be at least 20/100 (Snellen) in one eye and 20/70 (Snellen) in the other eye and must be corrected to at least 20/40 (Snellen) in one eye and 20/30 (Snellen) in the other eye. Applicants must be able to distinguish basic or saturated colors (lantern, yarn or other comparable tests). Hearing must be 12 feet, each ear. Both upper and lower extremities must be present in their entirety with the exception of the loss of toes or fingers which will cause no disability in the performance of duties.

A rigid physical examination will be made by a federal medical officer or other duly licensed doctor of medicine before appointment. Persons who are offered appointment must pay their own expenses in reporting for duty. If, on reporting at the place of assignment, they are found ineligible because of physical defects, they cannot be appointed and no part of their expenses for returning home can be borne by the government.

MEDICAL UNITS FOR SAN FRANCISCO

At the request of Angelo J. Rossi, mayor of San Francisco, two medical catastrophe units were shipped to that city on December 15 by the Medical and Surgical Relief Committee of America, 420 Lexington Avenue, New York. Arrangements are under way to send similar first aid medical and surgical units to hospitals in Maine, Vermont, South Carolina and New York, in response to requests. The new policy of the Medical and Surgical Relief Committee of America is to concentrate future activities on the furnishing of aid to American hospitals and other organizations where they require it for emergency use.

The Medical and Surgical Relief Committee of America is composed of some three hundred and fifty prominent physicians and surgeons. Its object is to make up shortages in surgical and medical supplies in America and, when necessary, to solicit donations for specific needs.

ORGANIZATION SECTION

OFFICIAL NOTES

THE ATLANTIC CITY SESSION

Special Exhibits on Fractures, Lame Backs, and Home and Hospital Delivery

The Committee on Scientific Exhibit announces that there will be three special exhibits at the Atlantic City session, as follows:

Special Exhibit on Fractures.—Presented by a committee composed of Dr. Kellogg Speed, Chicago, chairman; Dr. Frank D. Dickson, Kansas City, Mo., and Dr. Walter Estell Lee, Philadelphia.

Special Exhibit on Lame Backs.—Presented under the auspices of a committee composed of Dr. Frank R. Ober, Boston, chairman; Dr. Carl E. Badgley, Ann Arbor, Mich.; Dr. J. Archer O'Reilly, St. Louis; Dr. Arthur Steindler, Iowa City, and Dr. Philip D. Wilson, New York.

Special Exhibit on Home and Hospital Delivery.—Presented under the auspices of the Section on Obstetrics and Gynecology by a committee composed of Dr. Charles Edwin Galloway, Evanston, Ill., and Dr. Philip F. Williams, Philadelphia.

DOCTORS AT WORK BROADCASTS

Doctors at Work, the radio broadcast by the American Medical Association and the National Broadcasting Company, will continue uninterrupted through the holiday season.

The broadcasts are on the Red Network of the National Broadcasting Company and we are informed that approximately one hundred stations from coast to coast have signified their intention of taking the program.

The program features a dual theme, medical preparedness and "delay is dangerous." Under the first theme the relationship of doctors to the national emergency will be depicted, while under the second theme various medical situations and health situations in which delay may be disastrous to the patient will be illustrated.

As many as possible of the broadcasts are being relayed by short wave transmitters for rebroadcasting by the British Broadcasting Corporation, according to information received from the National Broadcasting Company.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Change in Status.—H. R. 6251 has passed the House and Senate, amending the Federal Food, Drug and Cosmetic Act by providing for the certification of batches of drugs composed wholly or partly of insulin, the certification to be under regulations to be promulgated by the Federal Security Administrator.

Bills Introduced.—H. R. 6229, introduced, by request, by Representative Rankin, Mississippi, proposes to provide liberalized benefits for disabled American veterans of the World War and their dependents. This bill provides, among other things, that the Administrator of Veterans' Affairs shall receive and adjudicate claims for World War emergency officers' retirement according to provisions of the Act of May 24, 1928, and where entitlement is established the Administrator is authorized to grant retirement as provided in that act. The benefits or privileges provided by the pending bill may not be denied because of failure to file claim within the period required by the 1928 act or because the former officer was not, prior to March 20, 1933, granted retirement pay. H. R. 6240, introduced by Representative Gillie, Indiana, provides that there shall be in the Medical Department of the Army, in addition to such assistants to the Surgeon General as are now authorized by law, an assistant with the rank of brigadier general, who shall be an officer of the Veterinary Corps. H. R. 6241, introduced by Representative Rogers, Massachusetts, proposes to authorize such sums as may be necessary to provide additional hospital and outpatient dispensary facilities for persons entitled to hospitalization in Veterans' Administration facilities.

MEDICAL ECONOMIC ABSTRACTS

HEALTH PLAN IN HOUSING PROJECT APPROVED

The comitia minora of the Medical Society of the County of New York has adopted a plan to provide four thousand four hundred tenants of the East River Housing Project, 446 East 104th Street, with the services of physicians at low cost, the New York *Times* reported, November 14. The plan calls for a two year experiment with voluntary cooperation of residents in East River houses. Twenty-five cents a month would be charged for single persons, 50 cents for a married couple, 75 cents for a couple with one child and $1 a month for a family of four or more. Subscribers would receive the unlimited services of a general practitioner, one resident physician being assigned for every two hundred and fifty families, or one thousand persons. Subscribers would have a free choice of any resident physician. The resident physicians would be selected by a supervising medical board of prominent physicians who are senior members of the staff of the nearest hospital. Resident practitioners would not accept private patients outside the housing area. The New York Foundation, a private fund, will assume all overhead expenses and guarantee each physician a minimum income of $1,500, but resident physicians caring for the full quota of two hundred and fifty families, or one thousand persons, would earn $3,000 a year. A board, consisting of two senior members of the medical board of a neighborhood hospital and two physicians appointed by the county medical society, would act in a supervising capacity and the project would be governed by the East River Medical Council, consisting of four members of the supervising medical board and two representatives of the tenants' association. Persons with catastrophic illnesses would not be taken care of by the plan but would continue to be referred to the wards of the local hospitals. Maternity care would be provided in hospitals as before, but antepartum and postpartum care would be provided by the resident physicians. To make physicians eligible to reside in a low cost housing project, the United States and city housing authorities would authorize one physician to reside on the project for every two hundred and fifty families. The project is similar to the plan placed in operation in 1940 for the tenants of the Vladeck Houses in the Corlears Hook section of New York City by the Medical Society of the County of New York.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 2283.

CALIFORNIA

Annual Surgical Meeting.—The Los Angeles Surgical Society held its twenty-fifth annual meeting, December 13. The guest speakers were Drs. Dallas B. Phemister, Chicago, and Stuart W. Harrington, Rochester, Minn. Dr. Phemister spoke on "Massive Resection and Transplantation for Selected Cases of Bone Sarcoma" and "Interruption of the Circulation of Bone and Its Surgical Significance" and Dr. Harrington discussed "Diagnosis and Surgical Treatment of Carcinoma of the Breast" and "Diagnosis and Surgical Treatment of Constrictive Pericarditis." Dr. James F. Percy, Los Angeles, was among the many local physicians on the program, speaking on "Surgery of Advanced Cancer of the Cavities of the Skull."

Annual Graduate Assembly.—The eighth annual postgraduate assembly of the Alumni Association of the College of Medical Evangelists was held at the White Memorial Hospital, Los Angeles, December 7. The speakers were:

Dr. Harold L. Thompson, Los Angeles, Gastroscopy.
Dr. Paul M. Hamilton, San Marino, Recent Advances in the Therapy of Communicable Diseases.
Dr. Thomas Addis, San Francisco, Diagnosis and Treatment of Nephritis in Group Practice.
Dr. Maximilian E. Obermayer, Los Angeles, Treatment of Pruritus.
Dr. Charles P. L. Mathe, San Francisco, Urinary Calculi—Management by the General Practitioner.
Dr. Erle Henriksen, Los Angeles, Sterility.
Dr. Robert A. Scarborough, San Francisco, Carcinoma of the Rectum.
Dr. Ben K. Parks, Long Beach, Otitis Media Complications Even with Chemotherapy.
Dr. Roy E. Thomas, Los Angeles, Atypical Pneumonia.
Dr. Douglas G. Campbell, San Francisco, Neurotic Personalities in General Practice.
Dr. Hans Lisser, San Francisco, Indications for and Modes of Administering Testosterone Compounds in the Male.
Dr. Rodney F. Atsatt, Santa Barbara, Physical Therapy in Care of Fractures.
Dr. Leo Eloesser, San Francisco, Compound Fractures in War Time.
Dr. Joseph Brennemann, Los Angeles, Clinical Significance of Abdominal Pain in Children.
Dr. Walter A. Bayley, Los Angeles, Diagnosis and Treatment of Acute Intestinal Obstruction.
Dr. Rupert B. Raney, Los Angeles, Surgical Treatment of Intestinal Obstruction.
Dr. Percival A. Gray Jr., Santa Barbara, Office Management of the Diabetic Patient.
Dr. William A. Boyce, Los Angeles, The Cross-Eyed Child's Problem.

ILLINOIS

Public Health Advisers.—The governor recently appointed the following to the board of public health advisers in the state department of health: Drs. Walter D. Stevenson, Quincy, Raymond W. McNealy, James H. Hutton and Robert S. Berghoff, chairman, all of Chicago. Dr. Clifford U. Collins, Peoria, was reappointed to the board, which serves in an advisory capacity to the state director of public health.

Chicago

New Koch Laboratory at Armour Laboratories.—Fred C. Koch, Ph.D., Frank P. Hixon distinguished service professor emeritus of biochemistry and recently retired as chairman of the department of biochemistry at the University of Chicago, will continue his researches in the field of endocrines at the Armour Laboratories, it is announced. A newly completed laboratory has been designated the F. C. Koch Laboratory and set up for his use in the chemical research department of the Armour Laboratories.

Research Fellowships at Illinois.—The Graduate School of the University of Illinois has established four research fellowships to be awarded for one year in medicine and dentistry at a stipend of $1,200 per calendar year, with one month's vacation. Fellows are eligible for reappointment in competition with new applicants. Candidates must have completed a training of not less than eight years beyond high school graduation. Candidates should indicate the field of research in which they are interested and submit complete transcripts of their scholastic credits, together with the names of three former science teachers as references. The fellowship year begins on September 1. Application blanks may be secured from the Secretary of the Committee on Graduate Work in Medicine, 1853 West Polk Street.

INDIANA

Malaria Control Program.—The state board of health is carrying out a malaria control program in defense industries located in widely separated areas with the assistance of a $90,000 appropriation by the WPA. The work is now in operation at Fort Benjamin Harrison, the Kingsbury Ordnance Works, near LaPorte, the Jeffersonville United States Quartermaster Depot, the Indiana Ordnance Works and Hoosier Ordnance Plant at Charlestown, the Jefferson Proving Ground near Madison and the army air base near Fort Wayne. In 1938 more than 1,000 cases of malaria were reported at Terre Haute, and in 1939 an outbreak occurred in a lumber camp in Lake County.

IOWA

Outbreak of Undulant Fever.—Up to November 13, sixty-three persons in Marcus, Cherokee County, had been found with positive reactions for brucellosis following an investigation of an outbreak in September involving thirteen persons. In the initial outbreak all the patients gave the history of using dairy products from a producer who distributed raw milk. Agglutination tests on dairy cows led to the discovery of three reactors and one suspicious reactor. The porcine strain of organism, Brucella suis, was isolated from milk specimens taken from two reactors. Blood cultures from some of the patients with undulant fever yielded the same organism. New cases subsequently reported were verified by positive agglutination reactions, and in addition twelve persons were found to have positive reactions in diagnostic dilution during a special survey among school children in public and parochial schools. Marcus has a population of 1,206.

LOUISIANA

Industrial Hygiene Section.—The Louisiana State Department of Health will establish an industrial hygiene section in its division of preventive medicine, beginning the first of the year. The U. S. Public Health Service will lend the new section personnel and equipment, according to *Industrial Hygiene*.

The Chaillé Oration.—The sixteenth annual oration in memory of Dr. Stanford Emerson Chaillé was delivered before the Orleans Parish Medical Society, New Orleans, December 2, by Dr. Roy R. Kracke, professor of pathology and bacteriology and chairman of the department, Emory University School of Medicine, Atlanta. His subject was the dangers of self medication with particular reference to analgesic drugs and their effect on the cellular constituents of the blood.

MARYLAND

Physical Examinations of the School Child.—Children entering kindergarten and the first grade of school in the Eastern Health District of the Baltimore health department are being given physical examinations this year in accordance with a new plan. School number 27 was selected for the experimental project, with the examinations being made by the family physician. New pupils whose families have no private physician or who cannot afford one will receive a complete examination by the school physician. Efforts are made to have the parents present during the examination. Pupils selected for reexamination will be those who show physical defects or health problems. The city health department reported in November that almost one half of the new pupils had been taken to family physicians who, in turn, had submitted forty-two reports on their examinations.

MASSACHUSETTS

Personal.—The Louis E. Kirstein Fellowship at Harvard Medical School, Boston, was recently awarded to Dr. Sidney Cohen, assistant in medicine at the school. Dr. Cohen graduated at Harvard in 1937.

Society News.—Dr. Nathan Finkelstein, Pittsfield, discussed "Renal Tuberculosis" before the Northern Berkshire Medical Society, November 6.——Dr. Augustus Thorndike Jr., Boston, discussed "Effects of Physical Therapy on Athletic Injuries" before the New England Society of Physical Medicine in Boston, October 22.——A special meeting of the Boston Health League was addressed, December 5, by Dr. Harold C. Stuart on "Nutrition in Occupied France."——Dr. Henry E. Sigerist, Baltimore, discussed "The Practice of Medicine in Historical Perspective" before the Greater Boston Medical Society,

December 2.——The Worcester District Medical Society was addressed, December 10, in Worcester, among others, by Drs. Edmund J. Croce, Worcester, on "Prothrombin Deficiency in Hemorrhage" and Edward Budnitz, Worcester, "Prophylactic Use of Sulfapyridine in Patients Susceptible to Subacute Bacterial Endocarditis Following Dental Surgery." Dr. Arthur H. Ruggles, Providence, R. I., discussed "The Problem Child of the 'Teen' Age" for the society in November.

MICHIGAN

The Max Ballin Lectures.—The Dr. Max Ballin Lectures, sponsored by the North End Clinic, Detroit, were delivered, November 26, by Drs. Mandred W. Comfort, Rochester, Minn., on "Disturbances of Physiologic Function in Pancreatitis and Their Recognition," and Robert Elman, associate professor of clinical surgery, Washington University School of Medicine, St. Louis, on "Surgical Aspects of Acute Pancreatitis."

Hospital Day.—Woman's Hospital, Detroit, observed "hospital day," December 3, with a special program: Drs. Charles F. McKhann, Ann Arbor, spoke on "Antenatal and Postnatal Influences on Physical and Mental Development of Infants"; Norman R. Kretzschmar, Ann Arbor, "Intrauterine Oxygenic Exchange"; Willis D. Gatch, Indianapolis, "So-Called Toxemias of Burns, Peritonitis and Bowel Obstruction," and William A. Scott, Toronto, some of the difficulties of gynecologic diagnosis. Preston W. Slosson, Ph.D., Ann Arbor, gave a talk at the banquet entitled "Europe's Extremity as America's Opportunity."

Society News.—Drs. Charles M. Henry addressed the Detroit Physiological Society, Detroit, November 13, on "Peritoneal Fluid in Peptic Ulcers"; Samuel J. Levin, "Absorption of Injected and Orally Administered Pollens," and Robert W. Bates, Ph.D., Difco Laboratories, "Recent Studies on the Pituitary and Growth in Dwarfed Mice." All are from Detroit. ——William R. Davis, D.D.S., director of the bureau of public health dentistry of the state department of health, Lansing, was installed as president of the Michigan Public Health Association at its meeting, November 13. He is the first dentist to hold this office. Emilie G. Sargent, R.N., director of the Detroit Visiting Nurse Association, was chosen president-elect.

MINNESOTA

Mayo Memorial Shrine.—A bronze statue of the late Drs. William J. and Charles H. Mayo in their surgical gowns will be the central point of interest of the Mayo Memorial Shrine to be erected in Rochester by residents of the city and Olmsted County, *Minnesota Medicine* announces. It will be placed on a granite base before a granite background in the central open space of an amphitheater, symbolic of operating rooms, it was stated. The shrine, designed by James Earle Fraser, New York sculptor, will be separate from that being planned by the Minnesota Memorial Commission. This commission was appointed by Governor Stassen late in 1940 to study the establishment of a $250,000 fund for a memorial to the Mayos. State Senator William B. Richardson, Rochester, is chairman of the commission, which is composed of seventeen representative citizens of Minnesota.

NEW JERSEY

Society News.—Dr. Martha M. Eliot, associate chief, U. S. Children's Bureau, Washington, D. C., discussed "Child Health in the Defense Program" before the Essex County Medical Society, Newark, November 13.——Dr. Lewis K. Ferguson, Philadelphia, addressed the Camden County Medical Society, Camden, on "Surgical Therapy in Lesions of the Large Bowel," December 2.

NEW YORK

Anthrax Among Mink—One Human Fatality.—The state department of health reports that 163 of 516 mink maintained on a farm were found dead on September 22. Pathologic and bacteriologic findings, reported by the State Veterinary College, Cornell University, Ithaca, showed that the animals had died of anthrax. The mink were owned by three persons and maintained in three separate units on the same premises. Since September 22 no mink have died and, according to their owners, none have been ill, *Health News* states. The district health officer followed up through local health officers all men who had handled the mink. One man who had skinned 100 of the animals was found on October 2 to have an anthrax lesion on his left middle finger below the nail. Antianthrax serum was administered, but the man died. All the carcasses of the animals were disposed of under the supervision of the state department of agriculture and markets. Only two of the pelts had been sold. These had been sent to a company in a city elsewhere in the state and were located there through the district health officer.

Instruction in Dermatology.—The Medical Society of the State of New York announces a course on dermatology, arranged by Dr. George M. Mackee, New York, for the Montgomery County Medical Society in Amsterdam. The lecturers, all of New York, are:

Dr. Frances Pascher, Brooklyn, Modern Conception of Allergy: Its Relation to Allergy, January 6.
Dr. Laird S. Van Dyck, Diagnosis and Treatment of Common Skin Diseases (exclusive of eczema, drug eruptions, cancer and syphilis), January 13.
Dr. Royal M. Montgomery, Modern Conception of Eczema with Special Reference to Dermatophytosis, January 20.
Dr. Elias W. Abramowitz, Drug Eruptions, January 27.
Dr. John Frank Fraser, Diagnosis and Treatment of Cutaneous Cancer and Precancerous Lesions, February 3.
Dr. Anthony C. Cipollaro, Cutaneous Tuberculosis and Allied Conditions, February 10.
Dr. Girsch D. Astrachan, Diagnosis, Cutaneous Manifestations and Clinical Course of Syphilis, February 17.

A monthly series of lectures opened October 23 with a talk by Dr. Alexander A. Weech on "Deficiency Diseases." Dr. Gaylord W. Graves spoke, November 24, on "Preventive Pediatrics and the Periodic Health Examination" and Dr. Charles L. Wood, "Blood Dyscrasias in Infancy and Childhood from the General Practitioner's Viewpoint," December 22. Dr. Katharine G. Dodge will discuss "Rheumatic Fever, Chorea and Heart Disease," January 26; Dr. Harry Bakwin, "Diarrheal Diseases, Acute and Chronic," February 23, and Dr. Philip M. Stimson, "Recent Developments in Communicable Diseases," March 23. This series is a cooperative effort between the state medical society and the state department of health. All the speakers are of New York.

New York City

Care of Aged Physicians.—At the annual session of the state medical society in April, the house of delegates voted to allow voluntary dollar contributions to the Physicians' Home to be added to payments of dues, to assist in the care of aged and infirm physicians. On November 29 the home had received about $5,000 from this source, it is reported. The Physicians' Home was founded in 1918 and reincorporated in 1936.

New County Bulletin.—The Medical Society of the County of New York plans to publish its own bulletin beginning the first of the year. At that time the *New York Medical Week*, heretofore published by the New York Medical Week, Inc., will cease to act as the official publication of the county society. The new publication will be known as the *Journal of the Medical Society of the County of New York*. The advertising manager's office will be located at 230 West Forty-First Street. All other communications should be sent to the journal at 2 East 103d Street.

Study of Pneumonia Extended.—With the opening on December 1 of a seven months study to include the general experience of physicians in New York County, the city department of health announces an extension of its investigation of pneumonia. Heretofore most of the data available for study have come from hospital records. In the current survey private practitioners have been asked to send in monthly reports, on forms furnished by the department of health, on all the pneumonia cases they treat. Information requested includes complete diagnosis, name of therapeutic agent, dosage and outcome, according to the *New York Medical Week*. The survey, available through Social Security funds, will be under the direction of Dr. Wheelan D. Sutliff, assistant director of the bureau of laboratories division of pneumonia control, city department of health.

New Cancer Hospital.—Ground breaking ceremonies took place, October 27, for the new Nightingale Hospital at 163d Street and Fort Washington Avenue, on land donated to the city by Presbyterian Hospital. The new three hundred and fifteen bed hospital will be devoted to the care and treatment of patients with cancer, to research into causes and methods of therapy and to the education of physicians, medical students and others in every phase of this disease. Columbia University College of Physicians and Surgeons will nominate members of the professional staff of Nightingale Hospital except such appointments as are made under the rules of the Municipal Civil Service Commission. The new hospital will replace the old New York City Cancer Institute Hospital on Welfare Island and the Cancer Clinic at 124 East Fifty-Ninth Street. It is expected that the hospital will be completed in March 1943 at a cost approximating $2,650,000.

NORTH CAROLINA

Electron Microscope Installed in Research Laboratories.—An electron microscope has been installed and put into operation in the laboratories of the division of experimental surgery of Duke University School of Medicine, Durham. This 1,500 pound machine develops 60,000 volts to magnify an object 25,000 to 100,000 times. It was built by RCA in Camden, N. J.

OHIO

Annual Cardiovascular Institute.—The Cincinnati Heart Council and the Academy of Medicine of Cincinnati held their eighth annual cardiovascular institute, November 18. Local physicians participated in the program of demonstrations, lectures and round table discussions. Dr. Homer F. Swift of the Rockefeller Institute for Medical Research, New York, gave the third in the Alfred Friedlander Memorial Lectures series on "The Nature and Etiology of Rheumatic Fever."

Personal.—Dr. Howard C. Stewart, Cleveland, tuberculosis coordinator for Cuyahoga County for three years and director of the county tuberculosis dispensary since it opened in July 1940, has resigned to rejoin the staff of the Tennessee State Department of Health, effective November 1.——Mr. Delmar R. Serafy, formerly executive secretary of the Columbiana County Public Health League and more recently with the National Tuberculosis Association, New York, has been appointed health education secretary for the Alliance Tuberculosis League and the Stark County Tuberculosis and Health Association.—— Dr. Irville S. Rian, Massillon, has been appointed medical superintendent of the Ohio State Sanatorium, Mount Vernon, to succeed Dr. Frank C. Anderson, who resigned to enter private practice.

PENNSYLVANIA

Society News.—Dr. Harold T. Brown, Pittsburgh, discussed "Findings in Pulmonary Tuberculosis" before the Fayette County Medical Society in Union, November 6.—— Dr. Herbert T. Kelly, Philadelphia, addressed the Cambria County Medical Society in Johnstown, November 13, on "Nutrition as It Applies to the General Diseases."——Dr. Edward J. Stieglitz, Garrett Park, Md., discussed "Problems of Aging" before the Washington County Medical Society in Washington, December 10.

TENNESSEE

Personal.—Dr. Kendall B. Corbin, associate professor of anatomy, histology and embryology at the University of Tennessee College of Medicine, Memphis, has been appointed chief of the division of anatomy, histology and embryology and acting head of the department of anatomy to succeed the late Dr. August H. Wittenborg, who also served as professor of anatomy at the school.

Society News.—Dr. August H. Lancaster, Knoxville, discussed "Congenital Syphilis" before the Knox County Medical Society, December 7. Dr. Henry C. Long, Knoxville, will speak before the society, December 30, on diabetes.—— The Shelby County Medical Society devoted its meeting, November 4, to a symposium on the use and abuse of drugs. The speakers were Drs. Arthur P. Richardson, James M. Bethea, James M. Brockman, Conley H. Sanford and Neuton S. Stern. All are from Memphis.——Dr. Murray B. Davis addressed the Nashville Academy of Medicine and Davidson County Medical Society in Nashville recently on "Appendicitis in Children."

Changes in Health Officers.—Dr. Derric C. Parmenter, Tupelo, Miss., has succeeded Dr. Thomas L. Harvey as head of the Dyer County health department, Dyersburg.——Dr. Raymond Mel Perry, Pasco, Wash., was recently appointed director of the Sevier County department of health, succeeding Dr. Lamar A. Byers, Sevierville, who is studying at Johns Hopkins University.——Dr. William L. Phillips, Centerville, director of the Hickman County health department, has been named registrar of vital statistics for the county.——Dr. Chester A. Hicks, Cochran, formerly with the Georgia State Department of Health, has been placed in charge of the Carter-Unicoi-Johnson counties health unit, Elizabethton.

TEXAS

In Memory of Dr. Bodansky.—A bronze plaque has been hung in the main building of the University of Texas School of Medicine, Galveston, in memory of the late Dr. Meyer Bodansky, who at the time of his death in June was professor of pathologic chemistry at the university. He had been a member of the faculty since 1919.

State Owned Cancer Hospital.—Recently enacted legislation provides an appropriation of $500,000 to construct a state cancer hospital. It is expected that the hospital will be at Galveston and operated in conjunction with the University of Texas School of Medicine, with Dr. John W. Spies, dean, in charge. The bill as passed had the endorsement of the state medical association, the state cancer committee, the state medical college, the Women's Field Army of the American Society for the Control of Cancer and the Federation of Women's Clubs.

WASHINGTON

Personal.—Dr. Charles E. Bender, formerly of Fostoria, Ohio, has been made assistant director of the student health service of the University of Washington, Seattle.

Society News.—The King County Medical Society devoted its meeting, November 3, in Seattle to a discussion of anesthesia; speakers were Drs. Dorthie Mae Ness Hopper, William A. Millington, Charles E. MacMahon and Quentin L. Wood. All are from Seattle.——Dr. Edwin A. Nixon, Seattle, discussed "Ligation and Injection Treatment of Varicose Veins" before the Spokane County Medical Society, November 13, in Spokane.

GENERAL

Postgraduate Assembly for Negro Physicians.—The sixth annual postgraduate assembly for Negro physicians will be held at Prairie View State Normal and Industrial College, Prairie View, Texas, March 2-5. The program will include lectures and clinics in tuberculosis, syphilis, heart disease, pediatrics and obstetrics by white and Negro physicians. There will be no registration fee, and any Negro physician licensed to practice medicine in the United States is eligible to attend. The assembly is sponsored by the Texas Tuberculosis Association, the Texas State Department of Health, the Lone Star State Medical, Dental and Pharmaceutical Association, the Prairie View state college, the Hogg Memorial Foundation of the University of Texas and the National Tuberculosis Association.

Foundation Benefits from Will of Founder.—Simon Guggenheim, at one time U. S. Senator from Colorado, who died, November 2, bequeathed the bulk of his estate to the John Simon Guggenheim Memorial Foundation, which he created in 1925 in memory of his son. After certain bequests to persons and institutions have been fulfilled, the foundation receives the residue of the estate and remainder and contingent interest in all the established trusts. The foundation was created to "promote the advancement and diffusion of knowledge and understanding and the appreciation of beauty." Since its establishment it has fostered research in the medical sciences through the award of fellowships. In 1941 a group of twenty fellowships was available for Latin American scholars for study in the United States, nine of which were in medicine and related fields.

Foundation for Eugenic Alleviation of Sterility.—Expanded activities of the National Research Foundation for Eugenic Alleviation of Sterility, Inc., Nesconset, N. Y., have been announced, which include the construction of new quarters, now nearing completion, and the publication of a year book. Lectures delivered during 1941 through the Society for Education in Heredity and Eugenics, under the auspices of the foundation, will be included in the year book. The National Research Foundation for Eugenic Alleviation of Sterility was organized in 1925 and incorporated in 1940. It aims "to reduce sterility in those eugenically sound; to that end to conduct research and to give suitable medical aid, to further education; to publish results and to initiate suitable legislation." Dr. Frances I. Seymour, New York, is medical director of the foundation.

Society News.—Dr. William L. Mann, Corpus Christi, Texas, was chosen president-elect of the Association of Military Surgeons of the United States at its annual meeting, November 1, and Dr. James A. Mattison, Glendora, Calif., was installed as president. Col. James M. Phalen, U. S. Army, retired, Army Medical Museum, Washington, D. C., is the secretary. The next annual session will be held at San Antonio on Nov. 4-7, 1942.——Dr. Harvey F. Garrison, Jackson, Miss., was named president-elect of the Southern Medical Association at the recent annual meeting in St. Louis. The 1942 meeting will be in Richmond, Va.—— The American Federation for Clinical Research will hold its annual meeting in Minneapolis, April 20-21, 1942. Dr. Thomas M. Durant, 3401 North Broad Street, Philadelphia, is the secretary.——Dr. Augustus C. Shipp,

Little Rock, was elected president of the Southern Tuberculosis Conference at the recent meeting in Asheville, N. C. Bernice Wright, New Orleans, is vice president and J. P. Kranz, Nashville, Tenn., secretary-treasurer.——The annual convention of Phi Lambda Kappa Medical Fraternity will be held in Philadelphia, December 29-January 1; additional details may be obtained from Dr. Benjamin B. Rittenberg, chairman of the convention committee, 5400 Arlington Street, Philadelphia.

Comparative Cost Estimated in Microfilm Service and Book Lending.—Atherton Seidell, Medicofilm Service, Army Medical Library, has published a report on the comparative costs of loan service and of microfilm copying in libraries. His analysis of the Medicofilm Service showed that in groups of one hundred orders the total expenditure for materials and work at the wage rate of $1 an hour was $17.25, or 17½ cents per microfilm. This included the handling of the books, the verification of the film copies and the mailing, but not the time required for keeping the accounts and collecting for the work done. Actual computations of personnel work hours and the time used in the handling of the 13,607 books lent on an annual average for the five year period 1936-1940 showed this cost to be appreciably higher than that of making and sending out microfilm copies. Mr. Seidell stated that from the standpoint of the borrower it is evident that those who have not yet become accustomed to using microfilms will object to receiving one instead of the book itself. Others will appreciate being able to keep the microfilm copy. The report states that from the standpoint of library operation, microfilm service has the advantages of permitting the collections to remain intact for their more uninterrupted use as well as reducing wear and tear of the books. A small charge for the microfilms would probably be sufficient to keep the expenses within the allotments for this feature of library service, making it possible for many reference libraries to extend their scope, it was stated. The report also pointed out that the lessened cost of rebinding books due to wear and tear in transit through the mails represents an important factor in estimating savings made by the wide use of microfilm.

Academy of Orthopaedic Surgeons.—The tenth annual convention of the American Academy of Orthopaedic Surgeons will be held at the Chalfonte-Haddon Hall Hotel, Atlantic City, N. J., January 11-15. Papers to be presented will include:

Dr. Edwin D. Weinberg, Baltimore, Two Cases of Late Rupture of the Extensor Pollicis Longus Tendon Following Colles's Fracture.
Dr. William A. Rogers, Boston, Treatment of Fracture and Dislocation of the Cervical Spine.
Drs. Frederic C. Bost and Verne T. Inman, San Francisco, Pathology of Recurrent Dislocation of the Shoulder; Report of Bankhart's Operative Procedure.
Drs. William T. Green and Sidney Farber, Boston, Eosinophilic or Solitary Granuloma—Is It a New Disease?
Dr. Robert L. Carroll, Los Angeles, Rate and Amount of Increase in Muscle Strength Following Infantile Paralysis.
Dr. Mather Cleveland, New York, A Study of Gross and Microscopic Lesions in Tuberculosis of the Spine.
Dr. William Allan, Charlotte, N. C., Prevention of the Hereditary Crippling Diseases.
Dr. Pedro Toledo, Havana, Cuba, What Is Actually the Best Treatment of Acute Osteomyelitis.
Drs. Philip Lewin and Louis Scheman, Chicago, Experimental Osteomyelitis.
Dr. Stuart A. Thomson, Toronto, Canada, Treatment of Club Feet with Dennis-Browne Splints.
Dr. Juan Farill, Mexico City, Extra-Articular Fixation and Bone Grafting of the Fractures of the Hip—Preliminary Report.
Drs. Ralph K. Ghormley and Markham B. Coventry, Rochester, Minn., Surgical Treatment of Painful Hips in Adults.
Dr. Wallace H. Cole, St. Paul, Further Report on the Kenny Treatment of Infantile Paralysis.

There will be other papers and courses on lame back, roentgen therapy, fractures, arthritis, knee joint, vitallium mold arthroplasty, bone metabolism, surgery of the hand, disability evaluation, foot disabilities, scoliosis, bone tumors, periarthritis of the shoulder, war surgery, club foot and congenital deformities. A motion picture program will be a feature each day of the meeting.

Encephalitis Research in Yakima Valley.—Mosquitoes have been proved one of the transmitting agents responsible for the spread of encephalitis and encephalomyelitis, the U. S. Department of Agriculture recently announced in reporting on a study carried on in Yakima Valley of Washington by specialists of the bureau of entomology and plant quarantine, staff members of the University of California Medical School, San Francisco, and Washington state and local health authorities. Nearly 10,000 mosquitoes, flies and other biting insects were collected this season and tested for viruses of the two diseases. The work was conducted in the Yakima Valley because 27 human beings and from 40 to 50 unvaccinated horses had encephalitis in that area during the summer of 1940. The insects were identified, frozen and shipped in solidified carbon dioxide to the San Francisco laboratory of the University of California, where they were divided into "pools" according to family and species, washed, ground and injected into mice. One pool composed of Culex tarsalis mosquitoes produced symptoms of St. Louis type encephalitis. Another pool of the same kind of mosquitoes produced the western equine encephalitis. The department of agriculture points out that, while it has been previously demonstrated that mosquitoes can transmit the disease under laboratory conditions, this is the first time that mosquitoes collected in the field have been proved to be carrying the disease virus. The particular species found carrying the virus is widespread in states west of the Mississippi. Further investigation aims to determine whether mosquitoes are the only transmitting agents of the disease in human beings, whether the Culex tarsalis mosquito is the only type that transmits the disease, whether mosquitoes must be abundant in order to cause the disease and whether mosquitoes harbor the disease between outbreaks. Successful vaccines for horses have been developed and are widely used but vaccination in human beings is not yet practical, it was stated. More than 3,000 cases of human encephalitis with about 9 per cent fatalities were reported this year by the U. S. Public Health Service.

CORRECTIONS

Izenstein Instead of Eisenstein.—Dr. Louis A. Izenstein of Springfield, Mass., writes that his name was misspelled in footnote 16 in THE JOURNAL, November 29, page 1847.

Leprosy in Canton.—In the Current Medical Literature department of THE JOURNAL, December 13, in the abstract "Leprosy in Canton," is the statement "Of the 52,000 inhabitants who came to the attention of the author, 84 (1.6 per cent) were found to show various symptoms of leprosy." The percentage within the parenthesis should have been 0.16.

Calculation of the Addis Count.—According to Dr. Ernest B. Zeisler of Chicago, the method of calculating the Addis count given in footnote 3 in the article by Pittinos, Craig and DeSanctis in THE JOURNAL, November 29, page 1855, contains an error. The first term in the numerator of the fraction reads "number of squares counted" instead of "number of casts or cells counted." The denominator reads "volume of area counted"; it is obvious that the authors mean "volume counted." Dr. Zeisler believes the formula could be amended as follows: Count the number of casts or cells, just as in a leukocyte count, in the four largest squares, namely 4 sq. mm., and call this n. Then the volume counted is 0.4 sq. mm. Now the formula for the total number of casts or cells per cubic centimeter in the twelve hour sample is

$$\frac{N = n \times 12 \text{ hour volume} \times 1{,}000}{0.4 \times 15/0.5}$$

or, briefly,

$$N = 83\tfrac{1}{3} \times n \times 12 \text{ hour volume.}$$

Government Services

New Facilities for Research in Aviation Medicine

A temporary building is now under construction adjacent to the laboratories of the Division of Industrial Hygiene, National Institute of Health, at Bethesda, Md., to house new facilities for research on problems of aviation medicine, according to *Industrial Hygiene*. This building is intended primarily for a new low pressure, low temperature chamber and accessory refrigerating equipment for the purpose of testing apparatus of all kinds used by aircraft personnel, including such items as oxygen equipment and clothing. The new decompression chamber is expected to provide simultaneous rapid lowering of temperature and pressure to simulate ascent from the ground at atmospheric pressure and 70 F. temperature to an altitude pressure equivalent to 45,000 feet and a temperature of —70 F. The rapid change of temperature and pressure obtainable will exceed that encountered in ascent by any modern aircraft. The only other installations of this kind now in operation are said to be at the Banting Institute, Toronto, and the other at Wright Field, Dayton, Ohio. In addition to the work on apparatus and equipment for aircraft personnel, studies are being made on the effects of sudden decompression to low pressures, the effects of anoxia and the influence of altitude exposure on visual function, it was stated.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 8, 1941.

Fitness of Men Examined for the Armed Forces

Medical examination has revealed a high rate of fitness among the men called up for the fighting services; eight out of every ten have been found fit and many more will probably "make the grade" after a few months of army life. A surprisingly high standard has been found in the age group 37 to 40; six out of ten have been found fit. During the past six months one fifth of the men originally placed in grade 3, the lowest category accepted by the services, have been reexamined and found so improved physically as to be posted to fighting units. Formerly they were serving as clerks, orderlies, batmen and store keepers. Instructions have been given that all grade 3 men are to be reexamined after a few months of army life. In grade 2 comparatively few men have been regraded. This grade is composed of men not quite up to the standard needed for fighting and whose condition does not improve with army training. They are, however, capable of strenuous duties.

Physical Standard of British Man Power

Age Group	Classification, Grade	Per Cent
18/19	1	78
	2	9
	3	3.7
20/25	1	72
	2	13
	3	8.6
35	1	52
	2	18
	3	10
36	1	49
	2	18
	3	11
37	1	46
	2	19
	3	12
38	1	44
	2	20
	3	13
39	1	41
	2	20
	3	14
40	1	37
	2	20
	3	15

The authorities have been agreeably surprised by the high standard of fitness of the older men. It was thought that men in their early thirties would show the effect of poor feeding in childhood during the last war and the sedentary lives they had led, but statistics disprove this. The accompanying table shows in percentages the physical standard of Britain's man power. Actual numbers cannot be given. The Germans claim that their men are far healthier than ours, but the fact is that their examination for army service is not so strict as ours.

Postwar Hospital Planning

The calmness with which the country views the most critical struggle in its history is indicated by postwar planning of many things. In the House of Commons the minister of health has announced that as soon as may be after the war the objective of the government will be to ensure that by means of a comprehensive hospital service appropriate treatment shall be readily available to every person in need of it. At present there are two distinct hospital systems—the voluntary and the municipal hospitals. The former are so called because they are supported by the voluntary gifts of the charitable to provide treatment for the poor. The municipal hospitals have grown out of the infirmaries provided for the same purpose by the authorities. Though now down to date they do not have the same reputation as the voluntary hospitals, to which the medical schools are attached. At present there is no coordination between the two systems. The minister of health said that it is proposed to lay on the major local authorities the duty of securing, in close cooperation with the voluntary agencies engaged in the same field, the provision of a coordinated service by placing on a more regular footing the partnership between the local authorities and voluntary hospitals. To achieve the best results and to avoid wasteful multiplication of accommodation and equipment it will be necessary to design such a service by reference to areas substantially larger than those of the individual local authorities. To avoid overlapping and uneconomical expenditure, the more highly specialized services at the teaching hospitals and other centers will serve the wider areas, and a proper division will be arranged between hospitals in these areas.

As to the financial aspects of the government's proposals, they intend to maintain the principle that in general patients shall be called on to make a reasonable payment toward the cost, whether through contributory schemes or otherwise. As far as any new burden may be thrown on local authorities in providing or maintaining hospital accommodation or in contributing toward the expenditure of voluntary hospitals, the government will make a contribution. Special arrangements for dealing with the teaching hospitals by way of increased educational grants are in contemplation. In present circumstances the arrangements for hospital services must be determined by war time requirements.

In a debate which followed, labor members demanded the abolition of the voluntary hospitals and the provision of a hospital service for every one by the state. But Sir Francis Fremantle, specialist in public health, said that in the voluntary system they had a wonderful service developed with extraordinary inequalities and deficiencies but also with extraordinary results, which had been the basis of our medical and public health work. Prof. A. V. Hill, physiologist, said that a high standard of humanity prevailed in our hospitals compared with foreign countries such as Germany. Neither *laissez faire* nor bureaucracy in themselves would suffice. It was necessary to find the best possible compromise between the two systems in medicine as in other matters. All concerned should refrain from playing politics and work together for the public good. Whatever form it might take, a universal public health service was necessary as regards both prevention and treatment. The world catastrophe through which we are passing will bring about many changes in this country, but probably only such as would have taken place much more slowly without it. Our hospital system is one of them. We prefer evolution to revolution and progress which conserves the past to destroying it. We can be charged with illogicality, but by our sturdy common sense we manage to secure practical results better than those of more logical peoples.

Red Cross Aid to Russia

A special Aid to Russia Fund has been opened by a committee of the British Red Cross, of which Mrs. Churchill, wife of the prime minister, is chairman. Speaking at a meeting of the fund Lord Iliffe, chairman of the executive committee of the Red Cross, said that we were assisting all our allies to the extent to which circumstances and geography permitted, but the help needed by Russia was on an altogether different scale in keeping with the enormous battle front. For this purpose they would aim at raising $5,000,000 within a reasonable time. Field Marshal Sir Philip Chetwode said that we had already sent over 140 tons of supplies to Russia and 53 cases of surgical outfits. We were in the closest touch with the American Red Cross in its mission to Russia. Lord Nuffield, the automobile magnate, has subscribed $250,000 to the Red Cross Aid to Russia Fund.

New Official Names for Drugs

One of the effects of the war is that we are producing synthetic drugs which formerly were imported from Germany and we are renaming them. The General Medical Council has issued a further list of approved names for drugs already produced or likely to be produced in this country. Amethocaine hydrochloride is the approved name for decicain, menaphthone for 2-methyl-1,4-naphthoquinone (menadione), perthidine hydrochloride for dolantin, soluble phenytoin for epanutin, eptoin, sodium diphenylhydantoinate, solantoin and soluble dilantin, sulfacetamide for albucid.

RIO DE JANEIRO

(From Our Regular Correspondent)

Nov. 18, 1941.

The Work of the Rockefeller Foundation in Brazil

The twenty-fifth anniversary of the beginning of the work of the International Health Board of the Rockefeller Foundation in Brazil has been enthusiastically commemorated. Besides articles in newspapers and in medical magazines, some medical associations have held special meetings to honor that humanitarian institution. The most brilliant of these meetings was one promoted by the oldest medical association of Brazil, the National Academy of Medicine. Under the chairmanship of Prof. Aloysio de Castro of the University of Rio de Janeiro Medical School the academy held a crowded meeting to honor the Rockefeller Foundation in the person of Dr. Fred L. Soper, its representative in Brazil. The principal speaker was Dr. Afranio Peixoto, professor of hygiene at the university, who reviewed the most salient facts in the services rendered by the foundation especially in the fields of medical education, public health nursing, instruction of sanitarians and the investigation and control of yellow fever, malaria and hookworm disease. Two medical commissions were sent to Brazil early in 1916, the first under Major Gen. William C. Gorgas, to study the yellow fever situation, and the second, composed of Drs. Richard M. Pearce, John A. Ferrel and Bailey K. Ashford, to survey the grounds of medical education, hospitals and dispensaries, public health agencies and sanitary progress. In the same year an effective cooperation began with the Brazilian National Department of Health and with the São Paulo University, growing little by little and leading to the great development resulting in the medical and public health institutions and services now in operation. One lasting result of this cooperation is the University of São Paulo School of Medicine, now housed in a magnificent building of many stories and provided with a faculty of distinguished professors. It is a long work begun with the cooperation of Drs. Samuel T. Darling and Wilson G. Smillie, whose services were an honor to American medical science. Today the São Paulo school is one of the best on the American continent, and its department of hygiene is a leading institute of scientific research in the country. In the field of public health too the cooperation of the Rockefeller Foundation was of the greatest value. The work against hookworm disease begun in 1916 and greatly developed since 1920 has led to the creation of many modern county health units. With the cooperation of the foundation in 1922 the first training school for nurses was founded in Rio de Janeiro, and a Nursing Division was started in the department of health of the city with an able body of ten American public health nurses as supervisors. This led to the creation of a few training schools for nurses in several cities of a large country where the professionally trained nurse was completely unknown before. The nursing service of the department of health of Rio de Janeiro is now an efficient and popular modern agency of health. With the help of the International Health Board of the Rockefeller Foundation, the School of Hygiene and Public Health of the Johns Hopkins University lent the services of two able professors, Drs. Allen W. Freeman and James A. Doull, to start a course of instruction for sanitarians in the medical school of Rio de Janeiro, and the foundation granted fellowships to many Brazilian public health workers, who went to the United States to study at leading American schools and to visit different public health organizations.

With the support of the Rockefeller Foundation a complete survey of the yellow fever situation developed in the discovery of the jungle form of the disease, the disclosure of sylvatic mosquito vectors other than Aedes aegypti (as Hemagogus capricorni and Aedes escapularis), the invention of the viscerotome as the leading means of postmortem diagnosis of yellow fever and, through the work of the Rockefeller Institute, the creation of an efficient vaccine, now injected into millions of people, thus protected against the sylvatic yellow fever, as the only practical prophylactic resource. Brazil is also indebted to the Rockefeller Foundation for the help in the fight against Anopheles gambiae, the worst vector of malaria, imported into Brazil from the west coast of Africa. Some species of anopheles are more susceptible to infection than others; some anopheles mosquitoes will not bite man at all; others will bite man only when other animals are not available. Anopheles gambiae of Africa, which had spread through the states of Rio Grande do Norte and Ceara, entering the great air port of Natal, Brazil, has probably the highest infectibility and the greatest preference for man of all Anophelines. This makes that species the most important vector of malaria in man. The intensive campaign against the gambiae conducted by the malaria service of the Brazilian health department with assistance in funds and personnel from the International Health Board of the Rockefeller Foundation is an outstanding example of "species sanitation." The measures concentrated on were those which would prevent the breeding of gambiae. The eradication of the imported Anopheles gambiae is a paramount example of what is possible through the use of modern antimalarial technic, available to the Brazilian health authorities through the invaluable cooperation of the Rockefeller specialists.

Professor Peixoto praised the humanitarian work of the Rockefeller Foundation in Brazil and commended Dr. Soper for his ability to win the friendship of Brazilian physicians, thus insuring once more the unity of the Americas.

Second Brazil-American Congress of Surgery

The second Brazil-American Congress of Surgery is meeting in Rio de Janeiro. The president of the congress is Prof. Benedicto Montenegro of the University of São Paulo, and the secretary general is Prof. Alfredo Monteiro of the University of Rio de Janeiro. The program includes as the main themes (1) the surgery of pain syndromes, (2) burns and (3) amputations from the functional point of view. The principal papers have been contributed by Drs. Jayme Poggi, Motta Maia and Barbosa Vianna of Rio de Janeiro, Drs. Mario Ottobrini, A. Correia Netto and Edmundo Vasconcellos of São Paulo, Dr. Julio Dietz of Buenos Aires and Dr. Manuel Riveros of Assunción, Paraguay.

Marriages

JOSEPH MCGUIRE, Dallas, Texas, to Miss Doris C. Nelson of Warm Springs, Ga., in Shreveport, La., November 3.

ARCHIBALD MAXWELL EDINGTON, Camp Borden, Ont., Canada, to Miss Marion Lowry of Ottawa, November 8.

SPRAGUE HEMAN GARDINER, Baltimore, to Miss Mary Sherret Biggers in Toledo, Ohio, October 22.

AUBREY LEIGHTON SPARKS to Miss Thetis Stiles Ashley, both of Warren, Ohio, October 6.

JEROME MORTON SPATZ to Miss Freyda Penner, both of Chicago, November 9.

ELI SILBERSCHEIN to Miss Moscha G. Weiner, both of Brooklyn, July 14.

Deaths

Robert Dawson Rudolf, Toronto, Ont., Canada; University of Edinburgh Faculty of Medicine, Scotland, 1889; F.R.C.P., London, England, 1910; professor emeritus of therapeutics at the University of Toronto Faculty of Medicine; served with the Canadian Army Medical Corps, with the rank of colonel, during the World War; at one time president and fellow of the American Therapeutic Society and of the Royal Society of Edinburgh; member of the Association of American Physicians; author of a textbook entitled "Medical Treatment of Disease"; aged 76; consulting physician to the Hospital for Sick Children and the Toronto General Hospital, where he died, November 2.

John Broadfoot Rae, New York; University of Glasgow Medical Faculty, Scotland, 1895; at one time professor of diseases of the ear at the New York Post-Graduate Medical School; member of the Medical Society of the State of New York, American Laryngological, Rhinological and Otological Society and the American Otological Society, Inc.; fellow of the American College of Surgeons; served during the World War; consulting aural surgeon, Manhattan Eye, Ear, Nose and Throat, Union and Riverside hospitals and Bronx Eye and Ear Infirmary; aged 74; died, November 20, in Douglas, Ariz.

Jesse Wright Downey Jr. ✙ Baltimore; University of Virginia Department of Medicine, Charlottesville, 1905; professor of otology at the University of Maryland School of Medicine and College of Physicians and Surgeons; member of the American Otological Society, Inc.; on the staffs of the Baltimore Eye and Ear Hospital, University of Maryland Hospital and the Mercy Hospital; consultant, United States Marine Hospital; aged 59; died, November 18, of hypertensive cardiovascular disease.

Robert Randolph Jones Jr. ✙ Durham, N. C.; Johns Hopkins University School of Medicine, Baltimore, 1928; assistant professor of surgery, Duke University School of Medicine; fellow of the American College of Surgeons; assistant surgeon, Duke Hospital; director of the Duke Tumor Clinic; director of education of the North Carolina Division of the Women's Field Army for the Control of Cancer; aged 39; was shot and killed by a deranged patient, November 18.

John Bruce Harvie ✙ Troy, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1881; formerly clinical professor of surgery at the Albany (N. Y.) Medical College; fellow of the American College of Surgeons; past president and secretary of the Medical Society of the County of Rensselaer; surgeon, Samaritan and St. Joseph's Maternity hospitals; consulting surgeon, Leonard Hospital; aged 84; died, November 14, of pulmonary edema and arteriosclerosis.

Elmer Marion Hansen ✙ Lincoln, Neb.; University of Nebraska College of Medicine, Omaha, 1927; member of the Central Association of Obstetricians and Gynecologists; on the staffs of the Lincoln General Hospital and Bryan Memorial Hospital; aged 48; died, November 12, of coronary disease in St. Louis while attending the convention of the Southern Medical Association.

Luther Curtis Ogle, Etowah, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1913; member of the Tennessee State Medical Association; formerly member of the board of education of Etowah and chairman of the county board of education; aged 52; died, November 9, of injuries received in an automobile accident.

Royall Roller Richardson ✙ Medical Inspector Commander, United States Navy, retired, Los Angeles; University of Virginia Department of Medicine, Charlottesville, 1899; entered the Navy June 3, 1901; retired March 1, 1935 for incapacity resulting from an incident of the service; aged 66; died, October 18.

William John Mulheran, Syracuse, N. Y.; Syracuse University College of Medicine, 1901; member of the Medical Society of the State of New York; on the staff of St. Mary's Maternity Hospital and Infants Asylum; aged 64; on the staff of St. Joseph's Hospital, where he died, November 7, of coronary thrombosis.

Belle Constant Eskridge, Monrovia, Calif.; Hahnemann Medical College and Hospital, Chicago, 1891; Harvey Medical College, Chicago, 1895; fellow of the American College of Surgeons; aged 82; died, November 9, of complications due to a fractured hip received in a fall.

James Allen Rutledge, Ada, Okla.; University of Louisville (Ky.) Medical Department, 1911; member of the Oklahoma State Medical Association; served during the World War; aged 52; died, November 2, of injuries received in an automobile accident.

John M. Clayland, Brooklyn; Medical College of Ohio, Cincinnati, 1884; member of the Medical Society of the State of New York; aged 81; died, November 23, in the Brooklyn Hospital, of subacute bacterial endocarditis.

Gus Bross Young, Des Moines, Iowa; Drake University College of Medicine, Des Moines, 1904; served during the World War; aged 59; died, November 5, at the Iowa Methodist Hospital of carcinoma of the stomach.

William Mathews, Philadelphia; University of Maryland School of Medicine, Baltimore, 1897; on the staff of St. Christopher's Hospital for Children from 1913 to 1930; aged 76; died, November 1, of arteriosclerosis.

Nathan Sherwood Ferris, Snow Hill, Md.; Georgetown University School of Medicine, Washington, D. C., 1910; served during the World War; aged 54; died, November 10, of carcinoma of the stomach.

Charles W. Murphey, Los Angeles; University of Louisville (Ky.) Medical Department, 1879; Medical College of Indiana, Indianapolis, 1882; aged 84; died, November 6, of cerebral hemorrhage.

Warren Lewis Hulse ✙ Detroit; Eclectic Medical College, Cincinnati, 1914; on the staffs of the Grace Hospital and the Highland Park Hospital; aged 60; died in November of coronary occlusion.

Emil Joe Pulkrabek ✙ Flatonia, Texas; Baylor University College of Medicine, Dallas, 1932; aged 38; died, November 3, in the Scott and White Hospital, Temple, of acute monocytic leukemia.

Thomas Jefferson McDaniel, Plymouth, Ill.; Rush Medical College, Chicago, 1886; aged 81; died, November 17, in St. Francis Hospital, Macomb, of bronchopneumonia.

Harry Marr Stoodley, Arlington, Mass.; Tufts College Medical School, Boston, 1904; member of the school committee; aged 63; died, November 5, of coronary occlusion.

Julius Abram Bogart ✙ Forrest City, Ark.; University of Arkansas School of Medicine, Little Rock, 1902; aged 72; died, November 17, of acute pulmonary edema.

George Francis Spencer, Atlantic City, N. J.; Jefferson Medical College of Philadelphia, 1920; aged 51; died, November 13, of atrophic biliary cirrhosis.

Mortimer Harwood Paine, Hanson, Mass.; Tufts College Medical School, Boston, 1909; aged 65; died, October 1, in Brockton of cerebral hemorrhage.

John B. Griffith, Lewistown, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1891; aged 85; died, November 15, of aortic regurgitation.

Edward Windsor Southall, Geneseo, N. Y.; Homeopathic Hospital College, Cleveland, 1879; aged 90; died, November 12, of chronic endocarditis.

Patrick O'Hair, Waverly, Minn.; State University of Iowa College of Medicine, Iowa City, 1880; aged 93; died, November 7, of heart disease.

Howard W. Pownall, Tyrone, Pa.; Jefferson Medical College of Philadelphia, 1879; aged 84; died, November 8, of angina pectoris.

Henry L. Uhler, Marion, Ohio; Jefferson Medical College of Philadelphia, 1883; aged 81; died, November 2, of coronary thrombosis.

Stephen Stevens, Exeter, Pa.; Bennett Medical College, Chicago, 1915; aged 60; died, November 11, of cardiorenal disease.

George Clarendon Shammo, Philadelphia; Baltimore University School of Medicine, 1898; aged 79; died, November 11.

William Clark Stockton, Milwaukee; Jefferson Medical College of Philadelphia, 1901; aged 68; died, October 23.

Herbert Beals, Buffalo; New York Homeopathic Medical College, New York, 1878; aged 86; died, November 18.

William Arthur Mitchner, Wilson, N. C.; Leonard Medical School, Raleigh, 1908; aged 59; died, November 5.

William Bartley Kyle, Athens, Ala.; Medical College of Alabama, Mobile, 1889; aged 78; died in November.

Roy C. Wolcott, Columbus, Ohio; Pulte Medical College, Cincinnati, 1897; aged 68; died, November 8.

Hector Guy, Miami, Fla. (licensed in Quebec in 1901); aged 67; died, November 14.

Bureau of Investigation

SOME MECHANICAL FRAUDS

Government Closes the Mails to Various Schemes

Fraud orders issued by the Post Office Department have frequently been the subject of extensive articles by the Bureau of Investigation in these pages of THE JOURNAL. Following are brief abstracts of some Fraud Orders not dealt with previously:

Albert Thurlow Hunt and his "Spine Relaxer."—Hunt, a Los Angeles osteopath, for some time sold through the mails what he called "Dr. Hunt's New Cervical Spine Relaxer." According to the Post Office memorandum on the case, the device was found to be a halter attached to rope pulleys and an overhead cross bar. It was to be suspended from a screw-eye at the top of a door and the user, seated below it, placed the broad strap under his chin and fastened the narrow, adjustable strap under the back of the head, using the straight edge of the buckle. He then grasped the free end of the cord above the head, causing a downward pull strong enough to put all the neck tissues on a vigorous stretch. This treatment was sold "for relief of the functional disorders of head, throat and neck, headache, insomnia, hay fever, nasal catarrh, catarrhal deafness, enlarged tonsils, sinus trouble, pyorrhea, eye troubles, goiter, apoplexy, neck, shoulder and arm neuralgia, and many other distressing conditions are benefited by the improved circulation which the Relaxer produces." The government produced expert medical evidence to show that none of these conditions are curable by any one device but require treatment based on their causes and manifestations. Although Hunt sent the Post Office Department a letter attempting to explain his alleged manipulative system of therapy, he neither appeared at the hearing of the case nor sent any one to represent him. His treatment was found to be a fraudulent scheme to obtain money through the mails, and on Jan. 10, 1940 it was accordingly debarred by a fraud order. Apparently Hunt thereafter used other means than the mails of shipping it, as the Food and Drug Administration at Washington announced on Nov. 28, 1940, that Hunt had been fined $50 for selling his "Relaxer" in interstate commerce with false and misleading claims on the label.

"Dr." T. B. Shrader and his "Ear Pump."—Shrader, a chiropractor, put out his device from Lincoln and Syracuse, Neb. It consisted of a red rubber suction cup with a soft sponge rubber face containing an opening so that the device might be placed over the ear. It was represented to restore or definitely improve the hearing of any deaf person regardless of the cause or duration of his condition or the failure of any other method; to overcome head noises, earache, dry ears and other "ear ailments" and to produce in all cases the same benefits as those claimed in the testimonials quoted in the sales literature. Neither Shrader nor any representative of his appeared at the hearing, at which the government presented an expert medical witness, a member of the staff of the Surgeon General of the United States. He testified that ear disorders may result from various causes on which a device like the Shrader "pump" would have no effect whatever or, if any, an almost negligible one. Its sale was accordingly declared to be a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises, and it was debarred from the mails by a fraud order issued on Oct. 14, 1940. (Shrader's Ear Pump was declared not acceptable by the Council on Physical Therapy of the American Medical Association, as reported in THE JOURNAL April 19, 1941, page 1771.)

Surehold Company's Truss.—"The Surehold Truss" was put out from North Quincy, Mass., and Westbrook and Portland, Me., by the Surehold Company, whose manager was a W. I. Kennedy. He is reported to have said that in 1936 he purchased the business from the estate of the original owner (not named), who had started the enterprise some fifty years before in Westbrook. It was found that neither Kennedy nor any one else connected with the business had any medical training. In addition to the device, the concern sold a nostrum "Rupturine" which was represented to relieve "outward irritation and pain." Although the truss was represented as a "cure" for hernia, an expert medical witness testified that it was not essentially different from, or superior to, other kinds of trusses but a simple spring-type device commonly used. The Post Office Department declared the sale of it a fraudulent means of obtaining money through the mails, and a fraud order debarring it was issued on June 28, 1940.

George W. Lowe's Sure Hold.—From Los Angeles one George W. Lowe sold through the mails what he called "Lowe's Sure Hold Appliance." This apparently had no connection with the "Surehold" truss dealt with in another paragraph, although from the government's description the two seemed to be similar. It is not surprising, therefore, that an expert medical witness testified that Lowe's device would not cure a hernia or hold it in place, as represented by Lowe in his use of customers' testimonials. It was even shown that in 1 case Lowe sold his appliance to a person who had definitely stated that he desired it for the cure of a hernia the size of a hen's egg. The business was debarred from the mails as a fraud on Oct. 2, 1940.

Oscillatherm.—This was put out by an A. E. Ovist and an O. L. Durham, an electrician and a chiropractor, respectively, trading as the Oscillatherm Company of Los Angeles, with a distributing branch at South Bend, Ind. They represented through the mails that their device when used as directed would safely, painlessly and effectively correct and overcome disorders of the prostate gland, restore that organ to a normal, healthy condition that would make surgical operations on the prostate unnecessary, and that it was the "best, safest and most effective" means available to the public for the correction of disorders in its field. The Oscillatherm was found to be an electrically operated mechanism to dilate and heat the rectum and massage the prostate. An expert medical witness for the government testified that a person without medical training would be incompetent to determine just what form of prostatic disorder he had, if any, or how to treat it either with the Oscillatherm or by any other method. The testimony further showed that the Oscillatherm would not effectively correct or overcome prostatitis or other prostatic disorders and that its use would be dangerous in cases in which cancer had already set in in causing the patient to delay scientific treatment. On Feb. 5, 1941, the Post Office Department issued a fraud order against the Oscillatherm Company, J. T. Wharton, manager, and their officers and agents. Thereafter, it appears, Ruth H. Welsh, who was said to manage the South Bend agency, sent out mimeographed form letters to former customers of the Oscillatherm Company informing them that their accounts had been assigned to her. On May 31, 1941 the Post Office extended the original fraud order to cover her name, as R. H. Welsh, on the ground that she was aware of the fraud order against the Oscillatherm Company and was deliberately seeking to circumvent and evade the provisions of it in mailing out the circulars mentioned.

STIPULATIONS

Agreements Between Federal Trade Commission and Promoters of Various Products

The following items are abstracts of stipulations in which promoters of "patent medicines," cosmetics or medical devices have cooperated with the Federal Trade Commission to the extent of agreeing to discontinue certain misrepresentations in their advertising. These stipulations differ from the "Cease and Desist Orders" of the Commission in that such orders definitely direct the discontinuance of misrepresentations. The abstracts that follow are presented primarily to illustrate the effects of the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act on the promotion of such products.

Agnes MacGregor, Inc., Cosmetics.—The Chicago concern that distributes these signed a stipulation with the Federal Trade Commission in February 1941 in which it promised to discontinue the advertising representations that any of the products in question will effectively cleanse enlarged pores, eliminate blackheads, prove a proper treatment for all types of acne, penetrate into the second layer of skin tissue, remove crow's-feet, wrinkles or fine lines, nourish the skin, promote the growth of new hair or correct dandruff.

Ambofa Hair Tonic.—This preparation, also known as "Ambofa Cream for Hair," is put out by the Ambofa Products Company, Hastings, Neb. In January 1941 this concern promised the Federal Trade Commission that it would discontinue certain misrepresentations in its advertising of the product. Among these were that it will make hair healthy, restore its natural beauty, color or luster, kill dandruff germs or rid the scalp of dandruff or eczema or prevent hair from falling or fading.

Approved Model Short-Wave Machine.—One Lillian B. Ferentz, trading as Wayne Short-Wave Company, Detroit, signed a stipulation regarding this with the Federal Trade Commission in January 1941. In this she agreed to cease representing that her device is a cure or remedy for sciatica, neuritis, lumbago, arthritis, rheumatism or sinus disorders or that it can be used for any purpose, unless it is clearly indicated that it cannot be safely used except under the supervision of a competent physician, and that its use is dangerous in cases of acute inflammatory processes such as nondraining cellulitis, acute arthritis and acute pelvic infection, and under other specified conditions; that the machine produces a "friendly fever" or that a fever can be created by using an electrical short-wave machine or that her device is identical with short-wave machines used by medical practitioners and hospitals.

Breck Preparations.—These are put out by John H. Breck, Inc., Springfield, Mass., which concern in March 1941 entered into a stipulation with the Federal Trade Commission. In this the company agreed to discontinue certain misrepresentations in the sale of "Breck's Hair Tonic" (designated by the numbers 1A, 1B or 3), "Breck's Lather-Oil pH8 Shampoo," "Breck's Special Scalp Cream," Breck's $1 Hair Cream," "Breck's $2 Hair Cream" and "Breck's Ointment." Among these were that any of the preparations, whether used alone or in combination, differs from other systems of treating hair and scalp troubles or is a competent remedy for eczema of the scalp, psoriasis, alopecia areata, headache, troublesome monthly periods or sick stomach; that any one of them is valuable for adhesions or will bring about a normal condition of the scalp-connective muscles, cause hair to grow, save the old hair, stop or prevent falling hair, atrophy or excessive loss of hair; cause, encourage or quicken the growth of hair, delay its graying, prevent the loss of hair following erysipelas, scarlet fever or other diseases or conditions or aid in restoring the hair in such conditions.

Chasers.—This breath lozenge is put out by Chasers, Inc., of New York. In January 1941 the concern stipulated with the Federal Trade Commission that it would cease advertising its product as "the one effective tablet" which would permanently overcome bad breath due to tobacco, onions, alcohol, garlic, organic derangements, infections and other conditions, do more than temporarily dispel such breath odors or kill or mask all types of unpleasant breath.

Dr. Cross' Health Shoes.—This misleading designation is to be discontinued in the sale of these shoes, according to a stipulation signed in April 1941 with the Federal Trade Commission by the Herbst Shoe Manufacturing Company, Milwaukee, and A. O., T. C. L. and Leroy D. Keehn, trading as Keehn Brothers, Chicago. These persons also agreed to cease using the word "Doctor" or the abbreviation "Dr." in connection with a name or with any other words as a trade name, brand or designation to imply that their products are made according to the design or under the supervision of a physician and contain special scientific or orthopedic features which are the result of medical determination or services. The company also agreed to cease using the term "Official Physical Health Director" or similar words which might give the impression that the shoes in question contain special or scientific features.

Dr. Kelly's Air-Flex Shoes and Dr. Kelly's Plastic Arch.—The "Dr." in these names which are stamped respectively on certain shoes for women and certain others for men is to be eliminated, according to a stipulation signed with the Federal Trade Commisison in April 1941 by C. W. Marks Shoe Company, Chicago, International Shoe Company and Samuels Shoe Company, Inc., St. Louis, and George E. Keith Company, Campello, Mass. It was agreed that the term "Doctor" or "Dr." might give the public the false impression that the products in question are made in accordance with a design or under the supervision of a physician and contain special scientific or orthopedic features which are the result of medical ideas.

Dr. Luther Nature Shape.—This name was stamped on the soles of shoes put out by Kepner-Scott Shoe Company, Orwigsburg, Pa. In April 1941 this concern promised the Federal Trade Commission to cease using the word "Doctor" in the brand name of its shoes, as this might give the false impression that they are made in accordance with the design or under the supervision of a physician and contain special scientific or orthopedic features based on medical authority.

Dr. Warren's Scientific Arch Support and Dr. Steward Arch Support Combination Last.—These devices were not, as represented by their names, made in accordance with the design or under the supervision of a physician and would not offer special scientific or orthopedic features based on medical determinations or services. In April 1941 the Charles Meis Shoe Manufacturing Company of Lebanon, Ohio, signed a stipulation with the Federal Trade Commission, promising to withdraw these misrepresentations from its advertising.

Cur-A-Ped.—This is put out by the Redolent Products Company of West Palm Beach, Fla. In April 1941 this concern stipulated with the Federal Trade Commission that it would discontinue advertisements which tend to convey the impression that the local application of its foot treatment would have therapeutic effects aside from those resulting from the product's analgesic properties, or significant value in destroying the deep burrowing fungi or ringworm, or offer any benefit other than temporary relief for tired, aching, burning, itching, tender, perspiring feet and cracked, inflamed toes or overcome superficial infection of athlete's foot. The concern also promised to cease representing that such specific bodily ailments as acute rheumatic fever, Bright's disease, diabetes, cirrhosis of the liver and other ailments are attributable to bad feet, or that treatment of foot disorders will correct such ailments.

Foley's Honey and Tar Cough Syrup.—Foley and Company, Chicago, signed a stipulation with the Federal Trade Commission in January 1941 in which it agreed to cease representing that this product has any therapeutic action in excess of temporary relief of coughing due to irritations of the throat and respiratory tract when these symptoms are due to mild inflammation of the mucous membranes of those structures or that it stimulates the irritated tissues of the bronchial tubes, other than their mucus-secreting glands, or will give continuous comfort to the user without continuous administration.

Foot-Pep.—This is promoted by A. Greenberg, H. Greenberg and Sol Bassan, trading as Foot-Pep Laboratories and Foot-Pep Sales, Chicago. In January 1941 these persons stipulated with the Federal Trade Commission that they would no longer advertise that "Foot-Pep" is a competent remedy for athlete's foot, that it has any therapeutic value in the treatment of this ailment in excess of giving temporary symptomatic relief or that it stops acidity, penetrates skin pores, stimulates foot circulation, "peps up" normal feet and soothes corns, bunions or calluses.

"Hair Culture."—This is the title of a book issued by Macfadden Book Company, Inc., New York. In March 1941 the concern promised the Federal Trade Commission that it would cease representing that the methods, advice or instructions set forth in the volume will, when observed and applied, prevent, correct the cause of or cure baldness, dandruff, brittleness, split or graying hair, prevent or stop falling hair when such condition is not caused by improper scalp hygiene, or will increase the strength of the hair.

Hex Tabs.—This is one of the nostrums put out by Edwin L. and Gordon Leisenring, trading as U. S. Drug and Sales Company of Denver. In January 1941 these persons promised the Federal Trade Commission that they would cease representing that "Hex Tabs" is a competent treatment for ailments of the kidneys, bladder, prostate or other glands.

H R 5.—Morris W. Hillinger, trading as Hilly Medicinal Products, Pasadena, Calif., promised the Federal Trade Commission in April 1941 that he would cease representing this as an effective treatment for conditions caused by overindulgence in alcoholic liquors and discontinue any advertisements that fail to reveal that there is potential danger in the use of such preparation by persons afflicted with organic heart trouble or high blood pressure and that it should not be used by such persons except on a physician's advice.

John A. Martin Products.—These are put out as hair and scalp treatments by one John A. Martin of Jersey City, N. J. In February 1941 this person promised the Federal Trade Commission to discontinue in his advertisements the use of such terms as "Nu Gro" and "Nu Hair," which terms might give the impression that his products will grow new hair, which the Commission claimed they will not do.

J. Goodman Products.—These consist of "Goodman's Forest Herb Tea Mixture," "Pinosan Pine Bath Salts" and "Silver Moon Brand Nerve Sedative Tea." In January 1941 J. Goodman, Inc., of New York promised the Federal Trade Commission to cease advertising that the first-named is an expectorant, that the bath salts stimulate the secretion of perspiration and that the tea is a sedative and a competent treatment for nervousness or sleeplessness. The concern also promised to cease using the words "nerve" and "sedative" or any other terminology representing or implying that the tea has any sedative effect on the nervous system.

Kloronol.—This nose drop is put out by one A. Marks, trading as the Sumlar Company, New York. In January 1941 the concern promised the Federal Trade Commission that it would discontinue advertisements representing that Kloronol may be continuously used without harm in certain pathologic conditions such as sinusitis or that fail to reveal that its continued or frequent use may cause nervousness, restlessness or sleeplessnes or that persons suffering from high blood pressure, heart disease, diabetes or thyroid trouble should not use the preparation except on competent advice.

Kohler Antidote.—This is put out by Kohler Manufacturing Company, Baltimore, which in January 1941 stipulated with the Federal Trade Commission that it would cease representing that its product "will relieve pain double quick, lightning fast, or quicker than other similar preparations;" that the preparation is absolutely safe, has no bad after-effects or that users can place absolute faith in it. In February 1941 a similar stipulation was signed by Courtland D. Ferguson, Inc., Washington, D. C., an agency handling the Kohler advertising.

Lydia E. Pinkham's Vegetable Compound.—According to a release issued by the Federal Trade Commission in January 1941, the Lydia Pinkham Medicine Company of Lynn, Mass., stipulated that it would cease representing that either "Lydia E. Pinkham's Vegetable Compound" or the tablets of the same name are of benefit to, or an effective remedy for, female functional disorders, menstrual aberrations or menopause in excess of relief of symptoms associated with and caused by menstrual aberrations and those associated with and caused by menopause and as a uterine sedative; that either product will benefit any symptoms or conditions that are due to organic disease; that either product will overcome melancholia, act as an aphrodisiac, enhance the attractiveness of the user, act as a general system tonic or afford permanent relief from nervousness, and that the liquid and tablets are fully identical in purpose and effect.

Mme. Grace McLendon's Hair Grower.—That this will stop falling hair, remove dandruff, prevent hair from turning gray, restore gray hair to its natural color or cause hair to grow were misrepresentations that Grace McLendon, trading as Grace McLendon's Hair Products, Pleasantville, N. J., promised to withdraw from her advertising when she signed a stipulation with the Federal Trade Commission in April 1941.

Newbro's Herpicide.—This hair preparation has been on the market for many years. Apparently, however, the first government action on it is that reported in a release issued by the Federal Trade Commission in January 1941. This states that Ar. Wimarick, Inc., trading as the Herpicide Company, New York, had agreed to discontinue certain misrepresentations in the advertising. Among these were that the product will prevent baldness or loss of hair, assure beautiful or healthy hair, penetrate pores, stir up sluggish scalp circulation or cause the sebaceous glands to function properly.

Requa's Oil for the Ear.—That the use of this will give immediate relief for stuffed-up ears, cause wax accumulations in the ear to dissolve quickly or almost instantly, do away with ear discomforts that may result in permanent deafness or offer any appreciable value as a massage oil for muscular pains and congestion when applied to cutaneous surfaces are misrepresentations that are to be discontinued in the advertising, according to a stipulation that the Requa Manufacturing Company, Inc., Brooklyn, signed with the Federal Trade Commission in April 1941.

Respirine.—This is put out by the Albert Laboratories, Inc., Chicago, which in January 1941 promised the Federal Trade Commission to cease representing that its product is an effective remedy for asthma, bronchial coughs, bronchitis or whooping cough; that it will do any more for these conditions than to afford temporary relief from accompanying symptoms; that it will relieve symptoms accompanying hay fever or constitutes a treatment for hoarseness, promotes healing, increases the flow of mucus from the nasal cavity, provides instant relief, represents a discovery or is safe, unique or distinctly new. The concern further declared that it had eliminated potassium iodide from its product since February 1940. In April 1941 Newby, Peron and Flitcraft, Inc., Chicago, an advertising agency, also signed a similar stipulation.

Valortone.—This was represented as a herbal treatment that would restore natural luster and loveliness to the hair and achieve results not obtainable from any other preparation. In January 1941 Julius Skinder, Clinton, Ind., operating under the trade names Valortone Herb Company and Lavelle Sales Company, stipulated with the Federal Trade Commission that he would withdraw these advertising misrepresentations and some others, such as that the product would enable users to regain natural color or health of hair or stop dandruff or falling hair.

Correspondence

MARRIAGE IN EPILEPSY AND DIABETES

To the Editor:—In a recent issue of THE JOURNAL (October 18, p. 1402) a query regarding the marriage of the epileptic was answered in a manner which I feel demands a protest. The reply ends "At present the only hope of eliminating the disease epilepsy is by birth control among epileptic adults." This reply overlooks two facts: The first is that a person afflicted with epilepsy who marries a normal person may expect one child in forty resulting from the union to suffer from convulsions. The second is that the hope of weeding out a recessive mendelian trait by birth control is so minute as to be negligible.

In interesting contrast is a letter with regard to the marriage of diabetic patients in the next issue (p. 1490). The reply states "If diabetes were to be eliminated by eugenics, not only diabetic patients but all relatives of diabetic patients would have to be sterilized or prevented from marrying." The commentator seems not alarmed to admit that some descendant of the proposed union would be likely to have diabetes. Need one be so alarmed that some descendant of a patient with epilepsy, or of the patient's relatives, will have convulsions? Epilepsy, like diabetes, can now usually be brought under control by proper medication if taken early enough. The medical profession should point the way to a more realistic attitude toward the disease and be willing to examine each case on its individual merits.

TRACY J. PUTNAM, M.D., New York.

SIR WILLIAM WILLCOX

To the Editor:—In THE JOURNAL of September 20 your London correspondent reported the death of Sir William Willcox and referred to his skill as a toxicologist, his great experience in forensic medicine, his connection with the Crippen case and his knowledge of chemical pathology, and mentioned his most important writings. He said nothing of his extraordinary and gallant services in the British army in one of its most terrible, fantastic but finally successful campaigns in World War I, that in Mesopotamia, from 1914 until after the official end of the war. The campaign was fought by what was officially the Indian, not the British, army—the Indian army composed of white British and native Indians. It was, of course, a part of the British forces but was really the Indian army, sent from India. The Mesopotamian War was a dreadfully difficult affair, replete with every kind of tragedy.

In the fall of 1914 the British occupied Basra, on the Shatt-al-Arab, the short river at the head of the Persian Gulf, formed by the confluence of the Tigris and the Euphrates. This meant war with Turkey. Conditions were difficult, the climate was atrocious, disease was common and local military actions were many; however, in the summer of 1915 the first advance was made up the Tigris against Baghdad. The army got as far as Ctesiphon but was from there driven back to Kut-el-Amara, where it was caught, besieged and captured. Things were in evil case anyway and made infinitely worse by the high incidence of scurvy and beriberi, which were not brought under control until the arrival of the special army consultants Sir Victor Horsley and Dr. (later Sir) William Willcox. Other diseases were present, heat stroke being the most fatal of all, undoubtedly causing the death of Sir Victor Horsley himself. The value of the work of Sir William during all this trying time cannot be exaggerated.

In 1917, with continued zeal in spite of all possible obstacles, the Indian army advanced a second time and captured Baghdad, where the commanding general, Sir Stanley Maude, shortly afterward died of cholera, which was there endemic. The undoubted reason for his death was that he had refused to take the immunizing inoculations against cholera, though he forced all his officers and men to do so; he claimed that a man of his age was immune. A furious controversy arose over his death, the accusation being made that Sir Stanley had been poisoned. Willcox, who had accompanied the troops and attended the general, testified that he was not poisoned; however, it took three months for a special board of inquiry to make up its mind that Sir William was right. Previous to his death General Maude had written of Sir William "I consider his work in improving the health of my forces equal to two divisions [about 30,000 men]. Whatever it costs in work and in money, you must see that the country provides everything that Willcox thinks necessary."

In 1918 more than 50,000 Christian refugees soaked into Mesopotamia from Turkey and Persian Azarbaijan; two thirds were Assyrians and one third Armenians. The Turks and the Kurdish tribes attacked and ravaged them when and where they could. The survivors were finally gathered in a camp on the Diyala River 3 miles from Baquba. The death rate was about 60 a day; typhus fever broke out "but was luckily recognized as such by the ever vigilant Colonel Willcox." To quote from the "Official Medical History:

> A large quarantine camp was formed, where all refugees were examined as a preventive measure. Few of the medical officers had seen cases of this fever, and, had the diagnosis not been made by the consulting physician at the time, the disease would probably have spread to the men of the labor corps.

Throughout the whole period of warfare and postwar readjustment a great service was done by the Order of St. John of Jerusalem and the British Red Cross Society, including its Indian branch. In writing of the work of these organizations Colonel Moens mentioned by name only one officer, Colonel William Willcox, "to whose labors the immense and progressive improvement in the health of the troops was so largely due, and by whose never failing help the Red Cross profited beyond all measure."

Throughout those trying years of warfare against men and disease, when death lurked on every side, Sir William carried on steadfastly and courageously while all about him companions died of battle casualties and sickness. The story of the devastating Mesopotamian War is now seldom thought of, but in all the firmament of military medicine the star of Sir William Willcox will shine as brightly as any other.

The notes contained in this letter have been obtained chiefly from the first of two volumes on Mesopotamia: I. "Loyalties—Mesopotamia 1914-1917; II. Mesopotamia 1917-1920: A Clash of Loyalties—A Personal and Historical Record," by Lieut. Col. Sir Arnold Wilson, K.C.I.E., C.S.I., C.M.G., D.S.O., formerly acting civil commissioner in Mesopotamia, political resident in the Persian Gulf, His Majesty's consul-general for Fars, Khuzistan, and so forth (London, Oxford University Press, Humphrey Millford, 1930 and 1931).

It is interesting to note the wide knowledge of this author and cavalry officer, born, brought up and educated in England, transferred to the Indian army and thence to Mesopotamia, who made, in his two fascinating volumes, free use of Latin, Greek, Biblical and other historical quotations. He put at the beginning, alone on one page as an invocation, a poem, "The Band in the Pines," which he found in the *Southern Illustrated News*, printed in 1863 during the U. S. Civil War, referring to the death of General Jeb Stewart's chief of artillery, Major Pelham, a gallant soldier killed at the age of 22.

RICHARD H. MILLER, M.D., Boston.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 16-17, 1942. Council on Medical Education and Hospitals, Sec., Dr. William D. Cutter, 535 North Dearborn Street, Chicago.

MEDICAL CORPS, UNITED STATES NAVY

Examination. Assistant Surgeon with the permanent rank of Lieutenant (junior grade) and Acting Assistant Surgeon with the probationary rank of Lieutenant (junior grade), Jan. 5-9. Examination will be held at the Naval Hospitals at Chelsea, Mass., Newport, R. I., Brooklyn, Philadelphia, Norfolk, Va., Charleston, S. C., Pensacola, Fla., Corpus Christi, Tex., San Diego and Mare Island, Calif., Puget Sound, Wash., Great Lakes, Ill., Pearl Harbor, T. H., and Naval Medical Center, Washington, D. C. Apply Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, December 20, page 2191.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Feb. 9-11. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, March 31. Final date for filing application is Dec. 31. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York City.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* April in advance of the meeting of the American College of Physicians and June, in advance of the meeting of the American Medical Association. Applications should be on file 6 weeks in advance of the date of oral examination. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: New York, June. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I. Group B.* Various centers, Jan. 3. *Oral. Part II. Groups A and B* Atlantic City, May or June. Final date for filing application is March 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral and Written. All Groups.* Philadelphia, June, preceding the meeting of the American Medical Association. Final date for filing application is March 1. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha, Neb.

AMERICAN BOARD OF PATHOLOGY: St. Louis, March 30-31. Final date for filing application is Jan. 30. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Cleveland, May 13, preceding the Region III meeting of the American Academy of Pediatrics. *Written.* Locally, February 14. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF RADIOLOGY: *Oral. All Groups.* Atlantic City, June 4. Final date for filing application is April 1. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written. Part I.* Various centers, March 2. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various centers, December. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Indiana June Report

The Indiana State Board of Medical Registration and Examination reports the written examination for medical licensure held at Indianapolis, June 17-19, 1941. The examination covered 15 subjects and included 100 questions. An average of 75 per cent was required to pass. One hundred and twenty candidates were examined, all of whom passed. One physician was licensed to practice medicine on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
College of Medical Evangelists		(1941, 2)	2
University of Southern California School of Medicine		(1940)	1
George Washington University School of Medicine		(1940)	1
Loyola University School of Medicine		(1940), (1941, 2)	3
Northwestern University Medical School		(1941, 3)	3
Rush Medical College		(1941)	1
University of Chicago, The School of Medicine		(1941)	1
University of Illinois College of Medicine		(1941, 2)	2
Indiana University School of Medicine		(1940), (1941, 97)	98
University of Louisville School of Medicine		(1941, 2)	2
University of Minnesota Medical School		(1941)	1
University of Oregon Medical School		(1932)	1
Medizinische Fakultät der Universität Wien		(1933)	1
Osteopaths*			3

School	LICENSED BY ENDORSEMENT	Year Grad.
Yale University School of Medicine		(1938)

* Licensed to practice surgery.

Virginia June Report

The Board of Medical Examiners of Virginia reports the written examination for medical licensure held at Richmond, June 17-20, 1941. The examination covered 8 subjects and included 80 questions. An average of 75 per cent was required to pass. One hundred and thirty-eight candidates were examined, 136 of whom passed and 2 failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
George Washington Univ. School of Medicine (1938),		(1940)	2
Howard Univ. College of Medicine (1939),		(1940, 2), (1941, 3)	6
Tulane University of Louisiana School of Medicine		(1941)	1
Cornell University Medical College		(1937)	1
Duke University School of Medicine		(1937), (1941)	2
Jefferson Medical College of Philadelphia		(1939)	1
Medical College of Virginia		(1938), (1941, 60)	61
University of Virginia Department of Medicine		(1941, 52)	52
Medizinische Fakultät der Universität Wien (1929), (1933), (1934, 2), (1937)			5
Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg		(1932)	1
Friedrich-Wilhelms Universität Medizinische Fakultät, Berlin		(1926)	1
Georg August-Universität Medizinische Fakultät, Göttingen		(1924)	1
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1925)	1
Osteopath*			1

School	FAILED	Year Grad.
Deutsche Universität Medizinische Fakultät, Prag		(1935)
Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau		(1923)

Twenty-seven physicians were licensed to practice medicine by reciprocity and 8 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners from February 13 through June 20. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Birmingham Medical College		(1910)	Alabama
George Washington Univ. School of Medicine		(1918), (1937)	Dist. Colum.
Georgetown University School of Medicine		(1934)	Maryland
Howard University College of Medicine		(1937)	Missouri
Emory University School of Medicine		(1922), (1930)	Georgia
Loyola University School of Medicine		(1927)	Ohio
Rush Medical College		(1935)	W. Virginia
University of Louisville School of Medicine		(1938), (1939)	Kentucky
Tulane University of Louisiana School of Medicine		(1928) (1937)	Mississippi, Louisiana
University of Nebraska College of Medicine		(1936)	Nebraska
Dartmouth Medical School		(1907)	New Hamp.
Cornell University Medical College		(1936)	New York
Univ. of Rochester School of Medicine and Dentistry		(1932)	Ohio
Ohio State University College of Medicine		(1938)	Ohio
University of Oklahoma School of Medicine		(1939)	Oklahoma
Jefferson Medical College of Philadelphia		(1925)	Penna.
University of Pennsylvania School of Medicine		(1928) (1936)	Penna., North Carolina
Medical College of the State of South Carolina		(1938)	S. Carolina
Meharry Medical College		(1940)	Tennessee
University of Tennessee College of Medicine		(1938)	Tennessee
University of Wisconsin Medical School		(1935)	Wisconsin
Osteopath †			Missouri

School	LICENSED BY ENDORSEMENT	Year Grad.
Yale University School of Medicine		(1934), (1936)
Georgetown University School of Medicine		(1934), (1936)
Tufts College Medical School		(1936)
Columbia University College of Physicians and Surgeons		(1929)
Duke University School of Medicine		(1935), (1937)

* Examined in surgery.

† Licensed to practice surgery.

Iowa June Report

The Iowa State Board of Medical Examiners reports the written examination for medical licensure held at Iowa City, June 3-5, 1941. The examination covered 8 subjects and included 100 questions. An average of 70 per cent in each subject was required to pass. Sixty-nine candidates were examined, 67 of whom passed and 2 failed. The following schools were represented:

School	PASSED	Year Grad.	Number Passed
Loyola University School of Medicine		(1941, 2)	2
State Univ. of Iowa College of Medicine		(1940), (1941, 57)*	58
St. Louis University School of Medicine		(1940)	1
Creighton University School of Medicine		(1940, 2), (1941, 3)*	5
University of Toronto Faculty of Medicine		(1939)	1

School	FAILED	Year Grad.
State University of Iowa College of Medicine		(1941)
University of Toronto Faculty of Medicine		(1939)

*Licenses have not been issued.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Governmental Hospital: Liability to Pay Patient.—The Welfare and Institutions Code of California authorizes the board of supervisors of each county to "establish and maintain a county hospital." Pursuant to that authority, the board of supervisors of Siskiyou County maintained a general county hospital in the city of Yreka, Calif. Patients of the hospital who were able to pay were charged for the actual cost of hospitalization; other patients were treated on a full charity or semicharity basis. There were no private general hospitals in Siskiyou County and consequently the county hospital accepted so many full pay patients that it operated at a financial profit. The plaintiff entered this hospital as a full pay patient for the treatment of a minor leg injury. During the course of the treatment, the plaintiff's leg was placed in a bake oven and left in so long that it was seriously burned and had to be amputated. In a subsequent suit against the county, and others, it was contended that the injuries were due to the negligence of certain nurses and doctors employed by the county hospital. The county demurred to the complaint, the trial court sustained the demurrer, and the plaintiff appealed to the district court of appeal, third district, California.

The defendant county contended that it was not liable for the plaintiff's injuries because, in operating the general hospital pursuant to statutory authorization, it was engaged in a governmental function. The plaintiff, however, contended that by making the charges so high that they resulted in the hospital operating at a financial profit, the county had abandoned its governmental function and entered the field of private business and that it was therefore engaged in a proprietary venture and should be liable for negligence to the same extent as a private institution. The district court of appeal said that the purpose of the statute authorizing the operation of county hospitals was to provide for the furnishing of hospitalization and medical care to persons who actually were in need of that care. Furthermore, the court observed, it was customary for county hospitals to accept pay patients so far as their facilities permitted. In Siskiyou County, because of the absence of any other general hospital, all persons requiring hospitalization were unable to get it, regardless of their ability to pay, if they were denied admission to the defendant hospital. Such persons were therefore actually in need of care, said the court, and the county was clearly at liberty to admit them to its hospital. Furthermore, the county had a right to compel each patient to pay as much of the actual cost of hospitalization as he could afford, and the imposition of a charge for services, even though incidentally resulting in a financial profit to the hospital, was not inconsistent with the exercise of a governmental function. *Davie* v. *Board of Regents*, 66 Cal. App. 693, 227 P. 243 (abstr. J. A. M. A. **84**:310 [Jan. 24] 1925). The district court of appeal therefore held that the county, in operating the hospital, was engaged in a governmental function and was not liable for the negligence of its employees. Judgment for the defendant county was accordingly affirmed.—*Calkins v. Newton, 97 P. (2d) 523 (Calif., 1939).*

Workmen's Compensation Acts: Refusal of Employee to Undergo Operation.—The employee injured his right knee and instituted proceedings to obtain compensation under the workmen's compensation act of Louisiana. An award was made, conditioned on the employee's submitting to an operation to correct his disability, to be performed by a surgeon of his own choice. This the employee refused to do and the matter came before the Supreme Court of Louisiana for review.

According to the record in this case, the injury to the employee's right knee consisted of a fractured internal semilunar cartilage which protruded to the medial side of the knee joint, causing a tumor mass or growth at that point. The testimony showed that the operation to relieve this condition would require the opening of the knee joint, making a split in the capsule and removing the loose or fractured portion of the semilunar cartilage. The employee contended that the lower court erred in holding that his disability could be relieved by a simple, minor and harmless surgical operation unaccompanied by great pain and unattended by serious risk. The employer argued that the refusal of the employee to submit to the tendered operation released the employer from the obligation to continue compensation payments, taking the position that when a simple and harmless operation which will cure the employee's condition is seasonably and duly offered and the employee arbitrarily and unreasonably refuses it, then that tender of the operation released the employer from the obligation of continuing compensation payments. The medical testimony in the case was in conflict as to whether the operation offered was a simple one, unattended by appreciable risk of pain. A physician called by the employer testified that the operation was comparable to an appendectomy or a tonsillectomy; he did not look on it either as a major or as a minor operation. This witness testified that it was little more than a minor operation and a little less than a major operation, something like removing a tumor from the abdomen. Another witness for the employer, an orthopedic surgeon, testified that in the hands of a competent orthopedic surgeon the operation was a simple one. He testified that from 75 to 80 per cent of persons undergoing such an operation recover completely without showing any weakness in the knee as a result of the operative procedure. He estimated the time of recovery from four to eight months and not exceeding one year. Another physician, who "did the medical work" for the employer, testified that the operation was a simple one because it is so common. The employee called only one medical witness, who testified that he would not consider the operation a minor one and seriously doubted whether the employee's knee would be as strong after the operation as it was prior to the injury.

The Supreme Court of Louisiana thought that if the tendered operation was to be regarded in the nature, as to the seriousness thereof, of a tonsillectomy, an appendectomy or an abdominal operation for the removal of a tumor, it certainly could not in the light of the jurisprudence of the state be considered such an operation that the employee's refusal to undergo it would be unreasonable and arbitrary. The court therefore held in effect that the employee was justified in his refusal to submit to the operation and affirmed the award of compensation after eliminating the requirement with respect to the operation.—*Simmons v. Blair, 194 So. 585 (La., 1940).*

Autopsies: Right of Insurance Company to Demand Autopsy After Burial.—The plaintiff insurance company insured the life of the insured under policies which provided, among other things, that in the event of the death of the insured "The Company shall have the right and opportunity to examine the body and to make an autopsy unless prohibited by law." The insured fell down a flight of steps and sustained a multiple fracture of the skull. Death followed within a few minutes. Two days later the decedent's administrator explained the facts surrounding the death to the insurer's agent, informed him that the funeral had been arranged for the afternoon of the following day and suggested that if an autopsy was desired it should be performed before the funeral because the widow would not consent to one after the interment. The agent indicated that an autopsy would not be required and the funeral took place as planned. Two weeks later, the insurance company requested an autopsy; the request was refused and the present suit ensued to establish the right of the insurer to exhume the body for the purpose of having an autopsy performed. The district court gave judgment for the insurer and the defendants appealed to the U. S. circuit court of appeals, fourth circuit.

The insurer contended that the exact cause of death of the insured was unknown but that there was reason to believe that it was due to the effects of intoxication. Two physicians testifying for the insurer, who had no knowledge of the physical condition of the deceased at the time of the accident and who had never examined him, stated that the insured might have died from coronary occlusion, arterial aneurysm, apoplexy or internal hemorrhage, that the use of alcohol by the insured would increase the likelihood that one of these diseases con-

tributed to his death and that the only way to be sure was by performing an autopsy. The evidence on the question of intoxication showed that the deceased was not inebriated at the time of his fall and that his general habits with respect to the use of intoxicants were "about the same as 90 per cent of the people who visit country clubs." Six physicians testified positively that the cause of death was a cerebral hemorrhage induced by the fracture. One of these, who had examined the insured two or three minutes after the fall and before his death, stated that the conditions present were inconsistent with either a coronary occlusion or an arterial aneurysm.

Some decisions, observed the circuit court of appeals, in construing a provision like that involved in this case have denied the right to an autopsy after burial unless the insurance policy specifically so authorizes, on the ground that "an unnecessary or unreasonable exercise of the right of autopsy entails a course of action that is abhorrent to the sensibilities of surviving relatives and may involve a desecration of the grave." The more modern rule, however, seemed to the court to be to permit an autopsy after burial if (1) it appears that, through no fault of the insurer, it was impracticable to demand and to perform the autopsy before interment and (2) it appears reasonably certain that an examination of the body will reveal something bearing on the rights of the parties which could not otherwise have been discovered.

The district court in this case found that one day only was available to the insurer between the death and the burial and that this was insufficient to permit an investigation. The demand for an autopsy two weeks after the death of the insured was, in the opinion of the lower court, made within a reasonable time. The district court also found that the insurer had reasonable ground to believe that an autopsy might disclose such a contributing cause of death as would relieve it from liability. Opinions may differ, said the circuit court of appeals, as to whether the period which elapsed after the insurer had knowledge of the death gave sufficient time before interment for a decision on the necessity of an autopsy. The appellate court did not consider it necessary to decide this point in view of the fact that the court was of the opinion that the insurer failed to show that it had reasonable ground to believe that death was not purely accidental within the meaning of the policies. All the evidence, the court continued, tended to show that the insured was killed by the fall and there was no evidence whatever to indicate that he was afflicted by any disease at the time of the accident. The insurer had no basis for its assertion, in the opinion of the court, that disease was a contributing cause of the death but only a hope that in the course of the investigation something might be revealed that would relieve it from liability. Under such circumstances, the court thought it would be unreasonable to compel the representatives of the deceased to permit an autopsy, and the judgment of the district court was reversed.—*McCulloch v. Mutual Life Ins. Co. of New York, 109 F. (2d) 866 (W. Va., 1940).*

Malpractice: Standard of Care and Skill Required of Specialists.—The defendant physicians specialized in diseases of children. On May 25, 1937 a mother, one of the plaintiffs, requested one of the defendants to call at her home to see her 9 month old son. He was unable to go but sent his office associate instead. The boy was found to be suffering from nausea, diarrhea and an inflamed throat. His temperature was 102 F. The condition was diagnosed as a common cold but two days later the boy's condition became much worse, his temperature rose to 104 F. and his breathing became so heavy that it could be heard downstairs. One of the defendants again examined the boy but advised the plaintiffs that their son just needed rest in bed and that hospitalization was not necessary. The next morning, however, the plaintiffs notified the defendants that they were taking their son to the hospital and requested the defendants to meet them there. The child was put immediately into an oxygen tent and subsequently a throat specialist performed an operation on the patient's throat, the nature of which was not disclosed by the record. The patient's condition continued to get worse, however, and he died two days later. Subsequently the plaintiffs, mother and father of the patient, sued the defendant physicians for malpractice. The jury found for the defendants, the trial court granted a new trial and the defendants appealed to the Supreme Court of Washington.

The trial court instructed the jury that the defendants were required to possess that degree of care and skill usually possessed by specialists engaged in a like practice in the same or similar communities. In other instructions, however, the jury was told that the defendants were to be held only to that degree of care and skill used by physicians generally at the time and in the locality. These instructions were obviously inconsistent. The defendants apparently conceded that a specialist is held to a higher degree of care than a general practitioner, but they contended that such rule applied only to physicians who specialized in the treatment of a particular disease or organ and not to a group specialty, such as pediatrics. The Supreme Court, however, failed to see any reason why physicians who specialize in the treatment of the diseases of children should not be held to the same degree of care that other physicians practicing the same specialty in the same community exercise. Since the instructions to the jury were conflicting, a new trial was proper, the Court said, because it was impossible to determine what effect such inconsistency may have had on the verdict of the jury.

The defendants further contended that the evidence was insufficient to justify the trial court in submitting the case to the jury. Malpractice, said the Supreme Court, need not be established by direct and positive evidence; circumstantial evidence will suffice. In this case there was a clear conflict in the testimony as to what was done. To the defendants' contention that there was no evidence from which the jury could find that the boy would have lived even though he had received prompt treatment, the Supreme Court replied that the plaintiffs were required only to show that the probability that the child would live was greater if he received prompt treatment than if he did not. There was sufficient evidence, in the opinion of the Court, to justify a submission of the case to the jury. The order granting a new trial was therefore affirmed.—*Atkins v. Clein, 100 P. (2d) 1 (Wash., 1940).*

Charitable Hospitals: Liability to Pay Patient.—While the plaintiff, a woman over 70 years of age, was a pay patient in the defendant hospital she fell out of bed and fractured her hip, the fall being attributed to the failure of one of the hospital's nurses to equip the bed with sideboards. The plaintiff subsequently sued the hospital for damages and obtained a judgment in the trial court. On appeal to the district court of appeal, the plaintiff's judgment was affirmed (87 P. (2d) 374; abstr. J. A. M. A. **114:**1406 [April 6] 1940) and the defendant appealed to the Supreme Court of California.

The defendant contended that it was a charitable organization, that there was no showing that it had failed to use due care in the selection or retention of its employees and that therefore it was exempt from liability for the torts of those employees. In the opinion of the Supreme Court, however, the more modern, as well as the more logical, view required charitable hospitals to respond in damages for injuries to a paying patient. The judgment for the plaintiff was accordingly affirmed.—*Silva v. Providence Hospital of Oakland, 97 P. (2d) 798 (Calif., 1939).*

Society Proceedings

COMING MEETINGS

Annual Congress on Industrial Health, Chicago, Jan. 12-13. Dr. C. M. Peterson, 535 North Dearborn St., Chicago, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 16-17. Dr. William D. Cutter, 535 North Dearborn St., Chicago, Secretary.

American Academy of Orthopedic Surgeons, Atlantic City, N. J., Jan. 11-15. Dr. Rexford L. Diveley, 1103 Grand Ave., Kansas City, Mo., Secretary.

American Orthopsychiatric Association, Detroit, Feb. 19-21. Dr. Norvelle C. LaMar, 149 East 73d St., New York, Secretary.

Pacific Coast Surgical Association, San Francisco and Del Monte, Calif., Feb. 17-20. Dr. F. L. Reichert, Stanford University Hospital, San Francisco, Secretary.

Society of American Bacteriologists, Baltimore, Dec. 29-31. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

Society of Surgeons of New Jersey, Trenton, Jan. 28. Dr. Walter B. Mount, 21 Plymouth St., Montclair, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1931 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

11:117-148 (Oct.) 1941

Goiter: Its Diagnosis and Treatment. J. M. Wilson, Mobile.—p. 117.
Congestive Heart Failure. W. Harbin Jr., Rome, Ga.—p. 120.
Surgical Complications of Peptic Ulcer. E. Drennen, Birmingham.—p. 123.
Cold in the Head: Its Effect on Sinuses. A. M. Walker, Tuscaloosa.—p. 125.
Idiopathic Hypocalcemia with Purpura: Treatment with Dihydrotachysterol. J. F. McDowell, Birmingham.—p. 128.
Syphilis in Private Practice, 1938 and 1940. C. K. Weil and H. J. Climo, Montgomery.—p. 130.

American Journal of Diseases of Children, Chicago

62:701-908 (Oct.) 1941

*Favism in Children. P. Robinson, Tel Aviv, Palestine.—p. 701.
Factors Influencing Retention of Nitrogen and Calcium in Period of Growth: IV. Effect of Estrogen. J. A. Johnston, Detroit.—p. 708.
Effect of Operative Procedures on Emotional Life of Child. G. H. J. Pearson, Philadelphia.—p. 716.
*Effect of Chemotherapy on Pneumonia in Infants Under One Year of Age. J. Greengard, Chicago; W. B. Raycraft, Oak Park, Ill., and W. G. Motel, Chicago.—p. 730.
McClure-Aldrich Test: Clinical Study and Evaluation. H. H. Lichtenberg, New York.—p. 743.
Incidence of Hypertrophic Pyloric Stenosis. A. Wallgren, Göteborg, Sweden.—p. 751.
*Intradermal Immunization: II. Diphtheria. M. L. Blatt, S. Fisher, and D. W. van Gelder, Chicago.—p. 757.
Sensitivity to Horse Serum Due to Previous Injections of Antigen. J. A. Toomey and W. P. Garver, Cleveland.—p. 765.
Infantile Amaurotic Family Idiocy: Its Relation to Niemann-Pick Disease and Other Disturbances of Lipid Metabolism: Report of Two Cases of Tay-Sachs Disease with Necropsy. J. L. Rothstein and Sara Welt, New York.—p. 801.

Favism.—Robinson states that in 1939 he encountered 5 cases of apparent Lederer's anemia but questioned the diagnosis when a year later his first 3 patients returned with the same disease. Shortly thereafter another patient was admitted to the hospital with the diagnosis of uremic coma. The history was typical of Lederer's anemia, but the mother mentioned that two days before the child, who was fond of the blossoms and the beans of Vicia fava, had eaten some uncooked beans. This detail brought favism to mind. Further questioning about the first 3 patients revealed that they had fallen ill on both occasions one or two days after eating broad beans. The other 2 patients seen in 1939 could not be traced, but in August 1940 a 12 year old boy and in January 1941 a 7 year old boy were admitted to the hospital with acute hemolytic anemia a day after they had eaten broad beans. Though favism has previously not been known in Palestine it seems probable that in some cases the illness diagnosed as blackwater fever was in reality favism. The pathogenesis of the disease is obscure. It occurs after the ingestion of uncooked or cooked beans and after inhaling the blossom dust. This, and the severe eosinophilia in the blood and the bone marrow, support the allergic theory.

Chemotherapy and Pneumonia.—Greengard and his co-workers point out that the mortality from pneumonia in children less than 1 year old in 1937 and 1938, before chemotherapy was used, was 32 and 31 per cent, respectively. From March 1939 to July 1940, 289 infants with pneumonia were treated. Eighty-nine of the patients were observed in 1939, when an attempt was made to control the experiment by selecting alternate patients for chemotherapy. The temperature became normal much more rapidly in the 46 infants treated with sulfapyridine; it reached normal by the fourth day, while in the 43 control patients the temperature was not normal until the seventh day. Likewise the average duration of illness and hospitalization of the treated group were distinctly less than that of the control infants. Also, the pneumonia of the patients receiving sulfapyridine usually did not extend to areas of the lung not involved on admission. All the 200 patients treated in 1940 were given sulfapyridine as soon as the diagnosis was made. The gross mortality among these infants was 10 per cent. Further classification shows that among infants from birth to 3 months the mortality in 1937 was 44 per cent, 46 per cent in 1938 and 12 per cent in 1940. Similarly, in the group from 3 to 6 months of age the mortality in 1937 was 26 per cent, in 1938, 40 per cent and in 1940, 16 per cent. For those more than 6 months old the mortality in 1940 was 7 per cent, in 1937 it was 27.5 per cent and for 1938 it was 22 per cent.

Intradermal Immunization.—Blatt and his collaborators gave intradermal injections of diphtheria toxoid to the 228 positive reactors encountered among 945 children from 1 day to 19 years of age. Of the 228 positive reactors, 151 received one or two intradermal injections of 0.1 and/or 0.2 cc. of alum precipitated toxoid and 77 received intradermal injections of 0.1 and then 0.2 cc. of plain unmodified toxoid purchased on the open market. Of the 93 children given 0.1 cc. of alum precipitated toxoid 48 were retested at the end of six weeks and 7 showed positive Schick reactions. Eleven months after immunization 4 of the 7 still had positive Schick reactions. Of the 38 given 0.1 and then 0.2 cc. of alum precipitated toxoid 36 were retested after eleven months and all had negative Schick reactions. Three of the 20 given two 0.2 cc. doses of alum precipitated toxoid showed positive Schick reactions nine months later and 1 child after sixteen months still had a positive reaction. Only 1 of the 77 children given plain toxoid intracutaneously had a positive reaction after nine months. Sixteen months after the last inoculation, 2 of the children had positive Schick reactions. Unmodified toxoid gave rise to less severe local reactions than alum precipitated toxoid. Therefore the preferred method of diphtheria immunization appears to be the intradermal injection three weeks apart of 0.1 and then 0.2 cc. of unmodified toxoid (Ramon's anatoxin). This should be followed by a third injection if the Schick reaction is still positive.

American Journal of Ophthalmology, Cincinnati

24:1105-1232 (Oct.) 1941

Role of Epinephrine in Formation of Intraocular Fluid. J. S. Friedenwald and W. Buschke, Baltimore.—p. 1105.
Experimental Transposition of Extraocular Muscles in Monkeys: Preliminary Report. P. J. Leinfelder and N. M. Black Jr., Iowa City.—p. 1115.
Protein Content of Aqueous Humor in Man. P. C. Kronfeld, Chicago.—p. 1121.
Histologic Eye Findings in Arachnodactyly. Georgiana Dvorak-Theobald, Oak Park, Ill.—p. 1132.
Glaucoma Associated with Hyaline Bodies (Drusen) of Optic Disk. A. G. Athens, Duluth, Minn.—p. 1138.
Tumors of Optic Nerve: Study of Thirteen Cases from Brazil, Diagnosis, Degree of Malignancy, Clinical Classification, Histopathologic Classification, Relation to von Recklinghausen's Disease, Methods of Surgical Treatment. J. Pereira Gomes, São Paulo, Brazil, South America, translated by C. A. Perera, New York.—p. 1144.
New Approach to Testing Eyes of School Children. T. H. Eames, Arlington Center, Mass.—p. 1170.
Retina and Intraocular Tension During Prolonged Insulin Coma, with Autopsy Eye-Findings. A. Gralnick, Central Islip, N. Y.—p. 1174.
Ocular Onchocerciasis. A. Quevedo, Guatemala, Central America, translation by F. A. Wies, New Haven, Conn.—p. 1185.

American Journal of Orthopsychiatry, Menasha, Wis.

11:619-808 (Oct.) 1941. **Partial Index**

What Can Psychiatry Contribute to the Alleviation of National and International Difficulties? F. Alexander, Chicago; L. K. Frank, New York; J. F. Brown, Lawrence, Kan.; W. Overholser, Washington, D. C., and G. Zilboorg, New York.—p. 619.
Fascism: Challenge to Mental Hygiene. H. S. Ephron, New York.—p. 652.
What Is a Normal Mind? N. Cantor, Buffalo.—p. 676.
Mental Hygiene in a Special Public School for Maladjusted Children. A. Blau and Louise Veo, New York.—p. 691.
Homosexual Trends in Children. Lauretta Bender and S. Paster, New York.—p. 730.
Treatment of Fearful Children. J. H. Conn, Baltimore.—p. 744.
Behavior Problems in Children with Syphilis: Relation to Juvenile Paresis. R. L. Jenkins and Myrtle Crudim, Chicago.—p. 752.
Runaways and Nomads. L. G. Lowrey, New York.—p. 775.

American Journal of Pathology, Ann Arbor, Mich.

17:643-784 (Sept.) 1941

Tribute to Dr. H. Gideon Wells, Investigator, Scholar, Teacher (Magister). A. B. Luckhardt, Chicago.—p. 643.
Epithelial Metaplasia in Congenital Cystic Disease of Lung: Its Possible Relation to Carcinoma of Bronchus. N. A. Womack and E. A. Graham, St. Louis.—p. 645.
Heredity as Determining Type and Site of Cancer and Age at Which It Occurs. Maud Slye, Chicago.—p. 655.
Nonsaponifiable Lipid Fraction of Livers from Cancerous and Noncancerous Persons. P. E. Steiner, Chicago.—p. 667.
Variation in Composition of Gallstones Simultaneously Formed in Gallbladder. D. B. Phemister and H. G. Aronson, Chicago.—p. 673.
Certain Specific and Immunopathologic Features of Tuberculosis. H. J. Corper, Denver.—p. 681.
Spread of Tubercle Bacilli by Sputum, Blood and Lymph in Pulmonary Tuberculosis. E. R. Long and R. Faust, Philadelphia.—p. 697.
Cavities in Silicotic Lung: Pathologic Study with Clinical Correlation. A. J. Vorwald, Saranac Lake, N. Y.—p. 709.
Age Factor in Active Immunization Against Whooping Cough. L. W. Sauer, Chicago.—p. 719.
Antigenic Relationship of Alcohol Soluble Substances of Corpus Luteum to Those of Testis and Brain. J. H. Lewis, Chicago.—p. 725.
Intrinsic Nerves of Immature Human Uterus. W. H. Brown and E. F. Hirsch, Chicago.—p. 731.
Some Factors in Development, Localization and Reabsorption of Experimental Amyloidosis in Rabbit. G. F. Dick and L. Leiter, Chicago.—p. 741.
Fatty Changes in Glomeruli of Kidneys. J. P. Simonds and J. D. Lange, Chicago.—p. 755.
Degeneration of Adrenal Cortex Produced by Germanin. Eleanor M. Humphreys and Lilian Donaldson, Chicago.—p. 767.
Acute Local Anaphylactic Inflammation of Lungs. P. R. Cannon, T. E. Walsh and C. E. Marshall, Chicago.—p. 777.

American Journal of Public Health, New York

31:1027-1120 (Oct.) 1941

Present Status of Venereal Disease Control Program in Mobilization and National Defense. R. A. Vonderlehr, Washington, D. C.—p. 1027.
What the Navy Is Doing to Protect Its Personnel Against Venereal Disease. F. R. Lang, Washington, D. C.—p. 1032.
Immunity and Positive Tuberculin Reaction. L. Brahdy, New York.—p. 1040.
Hospital Records as Source of Morbidity Statistics. Clara E. Councell, Bethesda, Md.—p. 1044.
Mortality Statistics and Physician: Argument for Classifying Deaths According to Informed Medical Judgment. J. V. DePorte, Albany, N. Y.—p. 1051.
Nursing Care of Sick as Part of Complete Nursing Service in Rural Areas. Helene B. Buker, Lansing, Mich.—p. 1057.
Appraisal of Nutritional Status. F. G. Boudreau, New York; C. E. Palmer, Washington, D. C.; W. M. Schmidt, Dorothy G. Wiehl and H. D. Kruse, New York.—p. 1061.

American Review of Tuberculosis, New York

44:377-508 (Oct.) 1941

Weather and Resistance in Pulmonary Tuberculosis: Part I. W. F. Petersen, J. S. Howe and M. E. Milliken, Chicago.—p. 377.
Cellular Reactions to Fractions from Tubercle Bacilli. Florence R. Sabin, Denver.—p. 415.
*Bilateral Tuberculous Pleural Effusions: Study of Forty-Five Cases. A. L. Paine, Ninette, Man., Canada.—p. 424.
Clubbed Fingers in Pulmonary Tuberculosis. R. H. Kaplan and L. Munson, Castle Point, N. Y.—p. 439.
*Follow-Up of 1,041 Tuberculous Patients. Margaret G. Stephens, New York.—p. 451.
Case Finding in Chinese Population of San Francisco. W. C. Voorsanger and G. B. Miller, San Francisco.—p. 463.
Pneumoperitoneum in Treatment of Pulmonary Tuberculosis. W. O. Fowler, Orlando, Fla.—p. 474.
Tuberculosis in Students. J. A. Myers, Minneapolis.—p. 479.

Bilateral Tuberculous Pleural Effusions.—Paine reviews the 45 cases of bilateral tuberculous pleural effusions encountered at the Manitoba Sanatorium during the last twenty years. In none of the patients was pneumothorax present. The author states that the bilateral involvement was not merely an effusion of the two sides but usually a manifestation of a widely disseminated infection in a person who had unusual powers of resistance but in whom all too often multiple foci of disease eventually developed. The prognosis in bilateral tuberculous effusion is distinctly more grave than in unilateral effusion. Aside from its being followed by a higher percentage of pulmonary tuberculosis, organs (besides the lungs) seldom affected in unilateral pleurisy are involved. Furthermore, often several organs become involved. Bilateral effusion is usually a manifestation of hematogenous infection and not infrequently of generalized miliary tuberculosis. This seems to explain why the presence or absence of pulmonary tuberculosis at the onset of pleurisy has no particular bearing on the subsequent tuberculosis in other organs and why sanatorium treatment apparently does not materially improve the prognosis.

Follow-Up of Tuberculous Patients.—Stephens states that the status of 1,041 tuberculous patients from the home office and field or sales force of the Metropolitan Life Insurance Company three years after their admission to a sanatorium was: Of the men in the minimal stage of the disease 83.8 per cent were able to work as compared with 30.2 per cent in the far advanced stage; of the women 77.6 and 12.7 per cent were able to work. After five and ten years the same results with regard to stage held true. Death from tuberculosis among persons in the minimal stage who were being cured was fairly infrequent even after the tenth year, when more than half of those with far advanced disease had died. The chances of recurrence among 761 ex-patients who completed their cure and were able to return to their work before December 1938 averaged for the men who were cured in the minimal stage 7.3 per cent per year for five years. This is equivalent to saying that 36.5 per cent of this group will have had a recurrence by their fifth anniversary of completion of cure (ability to resume occupation). For the women the average was 3.9 per cent per year, equivalent to 19.5 per cent in five years. The men in the moderately and far advanced stages had an average recurrence rate of 11.2 per cent per year, or 56 per cent in five years, as compared with 6.1 and 30.5 per cent for the women. These high readmission rates were experienced in spite of favorable conditions during the first cure and supervised rehabilitation. On the fifth anniversary of completion of cure 90 per cent of the ex-patients treated originally in the minimal stages of the disease were at work or were able to work, as compared with 75 per cent of those with advanced tuberculosis.

Archives of Internal Medicine, Chicago

68:663-850 (Oct.) 1941

Bronchiolitis Fibrosa Obliterans: Report of Case. J. S. LaDue, New Orleans.—p. 663.
Origin of Ketone Bodies from Fats and Their Regulation. S. Soskin and R. Levine, Chicago.—p. 674.
Acropachyderma with Pachyperiostitis: Report of Case. H. G. Brugsch, Boston.—p. 687.
*Acacia in Treatment of Nephrotic Syndrome: Influence of Acacia, Injected Intravenously, on Concentration of Proteins and on Colloid Osmotic Pressure of Serum. A. Goudsmit Jr., Philadelphia; M. W. Binger and Marschelle H. Power, Rochester, Minn.—p. 701.
Adrenocortical Compounds in Blood: Relation of Their Quantity to Arterial Hypertension, Renal Insufficiency and Congestive Heart Failure. W. Raab, Burlington, Vt.—p. 713.
Determination of Urobilinogen in Feces and in Urine: Comparison of the Sparkman and the Watson Procedure. C. J. Watson and Eleanor Bilden, Minneapolis.—p. 740.
*Direct Cultivation of Bacterium Tularense from Human Blood Drawn During Life and at Autopsy: Report of Three Fatal Cases of Tularemia, with Brief Notes on Two Others. J. C. Ransmeier, Nashville, Tenn., and Isabelle G. Schaub, Baltimore.—p. 747.
Gastroenterology: Review of Literature from July 1940 to July 1941. C. M. Jones, Boston.—p. 763.

Acacia in Treatment of Nephrotic Syndrome.—Goudsmit and his associates observed the changes of the serum proteins and the colloid osmotic pressure before and after the intravenous injection of acacia in 28 patients with the nephrotic syndrome. After acacia was administered the edema of 20 patients disappeared promptly, 3 patients with edema failed to respond with diuresis and in 5 no edema was present when treatment with acacia was begun. Statistical analysis of the data reveals a lack of correlation between diuretic response and changes of colloid osmotic pressure; for example, in 4 patients in whom a frank decrease of colloid osmotic pressure was observed the diuretic response was just as satisfactory as in 9 in whom the colloid osmotic pressure was definitely increased. The concentration of serum proteins usually diminished after injections of acacia; the average decrease was 22 per cent of the original concentration. The decrease could not be correlated with the amount of acacia given, the resultant concentration of acacia in the serum or the initial concentration of serum proteins. Increases in circulating plasma volume and concomitant dilution of the constituents of the plasma appeared to account adequately for the decrease of serum proteins. The gross changes in colloid osmotic pressure subsequent to treatment with acacia are directly related to the absolute changes of the

concentration of the serum proteins and of the concentration of acacia. In approximately half of the patients the calculated changes were within 6 mm. of the observed values. These changes were unrelated to the therapeutic effect.

Pasteurella Tularensis.—Ransmeier and Schaub discuss the data of 3 patients who died of tularemia and on whom necropsy was performed at the Johns Hopkins Hospital in December of 1937, 1938 and 1939, and data of 2 patients who died at Vanderbilt University Hospital in 1940. Pasteurella tularensis was cultured directly on blood-dextrose-cystine agar from the blood of 2 of the first 3 patients during life and from all 3 at necropsy. In addition, the organism was cultured from a pustule on a finger of 1 patient during life and from peritoneal fluid at necropsy and from the lungs of 2 post mortem. From 1 of the 2 other patients Past. tularensis was recovered by direct culture and by mouse inoculation from pleural fluid during life and by direct culture from heart blood at necropsy. The organism in the other patient was found on direct culture of the venous blood four days before death, in the pleural fluid three days before death and in the heart blood after death.

Archives of Pathology, Chicago

32:507-688 (Oct.) 1941

Genesis of Atherosclerosis. T. Leary, Boston.—p. 507.
Lipids in Kidney. R. H. Fuller, Cincinnati.—p. 556.
Pathology of Disseminated Lupus Erythematosus. P. Klemperer, A. D. Pollack and G. Baehr, New York.—p. 569.
Influence of Promin, Starch and Heptaldehyde on Experimental Leprosy in Rats. E. V. Cowdry and C. Ruangsiri, St. Louis.—p. 632.
Tuberculous Spondylitis: Histologic Study. B. N. E. Cohn, Denver.—p. 641.
*Postmortem Diagnosis of Allergic Shock: Value of Prausnitz-Küstner Reaction. H. Lund, Boston, and E. L. Hunt, Worcester, Mass.—p. 664.
General Pathology and Some Special Complications of Alcoholism. A. W. Wright, Albany, N. Y.—p. 670.

Postmortem Diagnosis of Allergic Shock.—Lund and Hunt established, by the passive transfer method, a diagnosis of allergy at the necropsy of a white woman following the injection of guinea pig protein. The patient, a ward maid in a hospital, had volunteered to serve as a control subject in an investigation in which normal and psychopathic persons were given intracutaneous injections of small amounts of guinea pig hemoglobin. At 9:09 a. m. she and many other volunteers received 0.2 cc. of a solution of guinea pig hemoglobin. Within a few minutes she complained of headache, and respiratory distress, wheezing and intense cyanosis set in. One subcutaneous and three intracardiac injections of epinephrine hydrochloride were given without avail. At 9:25 a. m. she was pronounced dead. All the volunteers were interrogated concerning past illnesses and particularly concerning allergy; the woman who died had withheld the information that she had heart disease and asthma. Despite the fact that sensitivity to guinea pig protein is not common and that the dose given was small, the authors felt that the most tenable explanation of their subject's fatal collapse was allergic shock. It seemed highly desirable to demonstrate whether or not there was in her blood a specific reagin to guinea pig hemoglobin. A specific sensitizing agent corresponding with the material injected was found in the blood serum by the technic of passive transfer. Further investigation revealed hereditary hypersensitivity, anaphylactic death of the patient's mother's cousin and asthma and hay fever in her mother. The deceased had no known contact with guinea pigs, indicating that the development of hereditary hypersensitivity does not necessarily require antecedent contact with the specific exciting substance.

California and Western Medicine, San Francisco

55:167-224 (Oct.) 1941

Surgery of Stomach and Duodenum. W. Walters, Rochester, Minn.—p. 175.
The Practitioner and Problems of Diabetes. R. F. Loeb, New York.—p. 182.
Intestinal Bleeding in Infants and Children. L. R. Chandler, San Francisco.—p. 187.
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Synthetic Estrogens: Clinical Experiences with Some of the Newer Forms. C. K. Canelo, San Jose, and H. Lisser, San Francisco.—p. 195.
Tribromethanol Nitrous Oxide Anesthesia: Its Use in Thoracic Surgery. J. H. Hutton, Portland, Ore.—p. 198.
Sulfanilamide in Ophthalmology. G. P. Landegger, Los Angeles.—p. 200.

Cancer Research, Baltimore

1:771-848 (Oct.) 1941

*Postirradiation Changes in Levels of Organic Phosphorus in Blood of Patients with Leukemia. J. C. Abels, J. M. Kenney, L. Craver, L. D. Marinelli and C. P. Rhoads, New York.—p. 771.
Isotopic Constitution of Potassium in Animal Tumors and Muscle from Tumor-Bearing Animals. A. Lasnitzki and A. K. Brewer.—p. 776.
Xanthine Oxidase (Dehydrogenase) Activity in Livers of Mice of Cancer Susceptible and Cancer Resistant Strains. F. H. J. Figge, and L. C. Strong, New Haven, Conn.—p. 779.
Transplantation of Leukemia Arising in Hybrid Mice. A. Kirschbaum and L. C. Strong, New Haven, Conn.—p. 785.
Effect of Testosterone Propionate on Mammary Tumors in Mice of C3H Strain. E. Elizabeth Jones.—p. 787.
Studies on Effect of Foster Nursing and Its Relation to Development of Mammary Carcinoma in Mouse. W. S. Murray, Buffalo.—p. 790.
Foster Nursing and Genetic Susceptibility for Tumors of Breast in Mice. J. J. Bittner, Bar Harbor, Maine.—p. 793.
Abnormalities of Breeding Behavior in Rats of the Albany (A-S) Strain. M. V. Danzi, Ethel Burack and A. W. Wright, Albany, N. Y.—p. 795.
Action of Yeast Extract on Transplanted and Spontaneous Malignant Tumors in Mice. R. Lewisohn, C. Leuchtenberger, R. Leuchtenberger, D. Laszlo and K. Bloch, New York.—p. 799.
Mechanism of Carcinogenesis: Study of Significance of Carcinogenic Action and Related Phenomena. I. Berenblum, Oxford, England.—p. 807.
Failure to Induce Sarcoma in Rats with Wheat Germ Oil Preparations. A. M. Brues, Boston, Beula B. Marble and B. Riegel.—p. 815.
Effect of Carcinogenic Hydrocarbons and Related Compounds on Autoxidation of Oils. H. F. Deutsch, D. L. Miner and H. P. Rusch, Madison, Wis.—p. 818.
Induction of Tumors in Rats by Carcinogens in Various Lipids. H. A. Davenport, J. L. Savage, M. J. Dirstine and F. B. Queen, Chicago.—p. 821.

Postirradiation Levels of Blood Phosphorus.—Abels and his associates state that the ingestion of subtherapeutic doses of radioactive phosphorus by 5 patients with leukemia was followed by a rapid increase in the concentration in the erythrocytes of the organic acid-soluble phosphorus compounds. Subsequently, an increased concentration in both the erythrocytes and the leukocytes was observed. This was not the case after the ingestion of nonradioactive phosphorus. To establish whether the change was due to the radioactivity of the phosphorus or to some chemical property of this isotope, the entire bodies of patients were irradiated and direct exposure of the cardiac area was resorted to to ascertain the change in organic acid-soluble phosphorus levels which followed. The irradiation of the whole body was administered by a 185 kilovolt machine at a distance of 500 cm. and at a rate of 0.4 r per hour. The cardiac irradiation was administered by a 150 kilovolt machine with 1 mm. of copper filter, at a distance of 60 cm. through a 10 cm. cone. The results, while qualitatively uniform, varied quantitatively from patient to patient, but the one binding characteristic in all patients was that there was a definite alteration of the organic acid-soluble phosphorus levels in the leukocytes, and usually of the erythrocytes, after all types of irradiation. The alterations following the ingestion of the phosphorus and the irradiation are probably due to the radioactivity of the isotope.

Florida Medical Association Journal, Jacksonville

28:101-148 (Sept.) 1941

Medicine and the Florida Criminal Law. F. H. Dieterich, Miami.—p. 115.
Pain Produced by Urologic Disease. R. B. Carson, Fort Lauderdale.—p. 120.
Use of Endocrines in Treatment of Functional Menstrual Disorders. T. H. Wallis, Ocala.—p. 122.
The Ways of Law and Medicine. S. Brittingham, Norfolk, Va.—p. 126.

Indiana State Medical Assn. Journal, Indianapolis

34:541-580 (Oct.) 1941

The Medical Front—Digest of Doctor's Situation. A. M. Mitchell, Terre Haute.—p. 541.
Sulfanilamide in Appendicitis with Abscess. M. N. Hadley, Indianapolis.—p. 543.
Influenza. R. A. Flack, Lafayette.—p. 544.
Suicide. J. J. Westra, Muncie.—p. 546.
Anorectal Diseases. H. H. Wheeler, Indianapolis.—p. 548.
Brachial Birth Paralysis. K. A. Fischer, Louisville, Ky.—p. 552.
Dr. Oliver Wendell Holmes—Some Unpublished Medical Case Records. C. L. Poston, Richmond.—p. 556.
Phonocardiograph Studies on Heart Diseases. H. N. Middleton, Indianapolis.—p. 559.
Nonmedical Reading for Physicians. H. J. Weil, Indianapolis.—p. 564.

Iowa State Medical Society Journal, Des Moines

31:457-510 (Oct.) 1941

Persistence of Function of Skin Grafts Through Long Periods of Growth. J. B. Brown and F. McDowell, St. Louis.—p. 457.
Prophylactic and Therapeutic Use of Oxygen in Surgical Patient. S. C. Cullen and J. E. Skewis, Iowa City.—p. 462.
Intratracheal Anesthesia in Head Operations. J. A. Thorson, Dubuque. —p. 465.
Severe Gastrointestinal Complication Following Use of Sulfapyridine. S. D. Maiden, Council Bluffs.—p. 472.
Hypertension: Modern Concepts in Diagnosis and Management. E. W. Anderson, Des Moines.—p. 475.
Use and Abuse of Sedatives. C. F. Obermann, Cherokee.—p. 478.
Some Problems in Anesthesia. Florence D. Johnston, Cedar Rapids. —p. 485.

Journal of Urology, Baltimore

46:147-354 (Aug.) 1941. **Partial Index**

Pathogenesis of Polycystic Kidneys: Reconstruction of Cystic Elements in Four Cases. R. F. Norris and L. Herman, Philadelphia.—p. 147.
Nephroscopy with Removal of Stone Following Nephrostomy for Obstructive Calculous Anuria. E. Rupel and R. Brown, Indianapolis.—p. 177.
Nephrolithiasis Complicating Chronic Ulcerative Colitis After Ileostomy: Report of Six Cases. W. W. Lindahl and J. A. Bargen, Rochester, Minn.—p. 183.
Incidence and Significance of Deposition of Calcium Plaques in Renal Papilla as Observed in Caucasian and Negro (Bantu) Population in South Africa. V. Vermooten, New Haven, Conn.—p. 193.
Perinephric Abscess: Review of 117 Cases. D. W. Atcheson, New Orleans.—p. 201.
Albuminuria from Standpoint of the Urologist. T. L. Howard, Denver. —p. 241.
Modern Methods of Handling Prostatic Obstruction: Evaluation of Transurethral Resection Based on 700 Cases. W. A. Milner and H. C. Engster, Albany, N. Y.—p. 278.
Relationship of Serum Acid Phosphatase Determination to Presence of Bone Metastases from Carcinoma of Prostate. C. C. Herger and H. R. Sauer, Buffalo.—p. 286.
Effect of Female Sex Hormone on Function of Human Testis. N. J. Heckel and C. R. Steinmetz, Chicago.—p. 319.
Comparison of Bactericidal Effect of Low Concentrations of Sulfanilamide and Sulfathiazole on Bacteria from Urinary Infections. H. F. Helmholz, Rochester, Minn., with technical assistance of Nora Larson. —p. 322.
Sulfapyridine Therapy in Treatment of Gonococcic Urethritis Resistant to Sulfanilamide. J. H. Semans, Baltimore.—p. 332.

46:567-806 (Oct.) 1941. **Partial Index**

Prognosis in Bilateral Renal Tuberculosis. W. F. Braasch and E. B. Sutton, Rochester, Minn.—p. 567.
Control and Arrest of Lesions of Renal Tuberculosis. G. J. Thomas, T. L. Stebbins, Minneapolis, and S. T. Sandell, Oak Terrace, Minn.— p. 579.
*Spontaneous Healing in Renal Tuberculosis. E. W. Beach and W. G. Shultz, Sacramento, Calif.—p. 590.
Apparent Cure of Hypertension by Nephrectomy. C. E. Burkland, Sacramento, Calif.—p. 638.
Hypertension: New Clinical Concept of Its Etiology. A. Ravich, Brooklyn.—p. 641.
Relation of Ureteral Length to Trunk Length and Body Height in Children. R. W. Coffelt and D. A. Charnock, Los Angeles.—p. 667.
Spastic Ureteritis (Ureteral Stricture): Essential Clinical Considerations. H. W. E. Walther and R. M. Willoughby, New Orleans.— p. 671.
Rectourethral Fistula Following Perineal Prostatectomy: Report of Four Cases. C. F. Rusche and S. K. Bacon, Hollywood, Calif.—p. 699.
Studies of Blood Loss During Transurethral Prostatic Resection. R. M. Nesbit and K. B. Conger, Ann Arbor, Mich.—p. 713.
Ten Years' Experience in Management of Cryptorchidism. V. S. Counseller, Rochester, Minn.—p. 722.
Studies in Malignant Testis Tumors: V. Tumors Developing After Orchidopexy: Report of Two Cases and Review of Sixty-Three. J. B. Gilbert, Schenectady, N. Y.—p. 740.
Crystallography of Urinary Sediments with Clinical and Pathologic Observations in Sulfonamide Drug Therapy. E. L. Prien, Boston, and C. Frondel, Cambridge, Mass.—p. 748.
Obstruction at Neck of Bladder Incorrectly Diagnosed as Neurogenic Bladder. J. R. Dillon, San Francisco.—p. 759.
*Urologic Complications of Cancer of Rectum. J. A. Seaman and C. Binnig, Springfield, Mass.—p. 777.
Additional Uses for Tidal Drainage. W. G. Hayward, Jamestown, N. Y. —p. 793.
Oliguria: Review of Five Cases. W. D. Warrick, Birmingham, Ala.— p. 799.

Spontaneous Healing in Renal Tuberculosis.—To prove the contention that spontaneous clinical or objective healing may and does occur in patients with early renal tuberculosis, that is before caseation or extensive anatomic changes take place, Beach and Shultz report the histories of 8 such patients who were under their supervision for six to fifteen years. As signs of tuberculosis elsewhere in the body were absent, diagnosis of renal tuberculosis depended on the recovery and identification of tubercle bacilli from the urine from one or both kidneys. Varying numbers of pus cells and erythrocytes were always present in the urine from the bladder. Urologic study was usually suggested by the discovery of pus in the urine. During the periodic follow-up examinations of these 8 patients the objective findings or subjective symptoms have not recurred, and in their absence the authors feel justified in concluding that the tuberculous renal lesion or lesions from which these persons suffered at first healed spontaneously.

Complications of Cancer of Rectum.—Seaman and Binnig say that, of 111 patients with cancer of the rectum seen at the Westfield State Hospital from December 1937 to April 1, 1941, 68 were available for preoperative and postoperative observation. The ages of the patients ranged from 20 to 79; 41 were men and 27 women. Eighteen of the men had frequency or urgency of urination or burning during urination. Most of the women complained of some degree of frequency. However, it was not attributable to the rectal growth; leukorrhea was believed to be responsible in nearly all of them. A combined abdominoperineal operation of the one stage Miles type was performed in 42, 6 had the two stage Lahey operation, 4 had a Mikulicz procedure, 8 had posterior resection and the others had modifications of these operations. Postoperatively 2 had pronounced stricture of the deep part of the urethra, 4 had perineovesical fistula, 1 had ureterovaginal fistula, most patients had infection of the bladder, 1 had a ureter tied off accidentally during the perineal part of a resection, 3 had hydronephrosis on the right and 3 on the left side, 1 had pyonephrosis, 2 had infected hydronephrosis on the right side, many patients had dysfunction of the bladder (but no complete neurogenic conditions), and sexual potency, if still possessed before surgical intervention, was lost permanently afterward. There were 2 instances of epididymitis. Urologic complications vary in occurrence and severity, and they are more often due to sympathetic or parasympathetic destruction or some degree of trauma, possibly also to infection. Infection, because of the nerve disturbance and the altered position of the base of the bladder, is a common attendant.

Kansas Medical Society Journal, Topeka

42:369-412 (Sept.) 1941

Cancer of Rectum. N. A. Womack, St. Louis.—p. 369.
Nicoll Flap Operation for Empyema. B. A. Nelson, Manhattan.—p. 374.
X-Ray Studies of Female Pelvis. A. Brown, Salina.—p. 378.
Management of Edema and Nephritis in Children. J. H. Bena, Pittsburg.—p. 382.
Changes in Blood in Tubal Pregnancy. M. A. Walker, Kansas City. —p. 385.
Enterococcic Endocarditis Due to Streptococcus Fecalis: Report of Two Cases. T. R. Hamilton and Bette Wasson Hamilton, Kansas City. —p. 388.

Kentucky Medical Journal, Bowling Green

39:369-404 (Oct.) 1941

Responsibilities of Medicine. E. L. Henderson, Louisville.—p. 372.
Changes in Surgical Treatment of Peptic Ulcer. G. Aud, Louisville.— p. 377.
Epilepsies. T. Scott, Lexington.—p. 381.
Newer Applications of Peritoneoscopy and a New Instrument to Aid the Procedure. J. E. Hamilton, Louisville.—p. 387.
Trichinosis: Case Report. J. E. Winter, Louisville.—p. 391.
Medical Monuments. J. M. Salmon, Ashland.—p. 393.
Malignancy. H. C. Chance, Pineville.—p. 397.
Analysis of Thirty-Seven Cases of Syphilis. T. A. Griffith, Mount Vernon.—p. 400.

Laryngoscope, St. Louis

51:821-902 (Sept.) 1941

Otogenic Complications: Résumé and Discussion of Literature for 1940. L. G. Richards, Boston.—p. 821.
Analysis of Speech Characteristics in Deafened Children, with Observations on Training Methods. W. Hughson, A. Ciocco, E. G. Witting and P. S. Lawrence, Abington, Pa.—p. 868.
Otogenous Tetanus. S. Rosen, New York.—p. 892.
Right Upper Lobe Bronchoscopy—Position That Facilitates the Procedure. W. B. Faulkner Jr., San Francisco.—p. 894.

Maine Medical Association Journal, Portland

32:205-224 (Sept.) 1941

Clinical Study of Obstetric Paralysis. C. W. Ruhlin, Bangor.—p. 205.
The Word Is Cause, Doctor. P. B. Stinson, Augusta.—p. 209.

32:225-250 (Oct.) 1941

Review of Literature on Blood and Plasma Transfusions. J. E. Porter, Portland.—p. 225.
What Is Dementia Precox? I. Newman, Augusta.—p. 231.
Congenital Factors in Urinary Infections. S. N. Vose and F. P. Morse Jr., Boston.—p. 236.

Michigan State Medical Society Journal, Muskegon

40:761-840 (Oct.) 1941

Adjustment of Marital Problems. L. S. Selling, Detroit.—p. 789.
Uterine Fibroids Complicating Pregnancy. J. R. Willson, Ann Arbor.—p. 795.
Varicose Veins: Allergic Reactions in Injection Treatment. S. Rosenzweig, M. Ascher and L. Zlatkin, Detroit.—p. 800.
Method for Correction of Angulation in Fractures of Long Bones. V. M. Moore, Grand Rapids, and P. A. Van Pernis, Chicago.—p. 806.
Severe Fractures of Ankle Joint: Conservative Management and Presentation of Typical Cases. H. C. Lavender, Kalamazoo.—p. 807.
Hypothyroidism in Children: Review of Masked Symptoms and Evaluation of Response to Thyroid Treatment. A. M. Hill and J. E. Webber, Grand Rapids.—p. 811.
*Progressive Pseudohypertrophic Muscular Dystrophy: New Regimen of Treatment. H. E. Branch, Flint.—p. 814.
Sarcoma of Urinary Bladder: Report of Case. W. E. Keane, Detroit.—p. 823.

Pseudohypertrophic Muscular Dystrophy.—Branch based the following regimen on the five important facts (increase of creatine in the urine, gradual replacement of degenerating muscles by fatty infiltration, decrease or absence of magnesium in the muscle, decrease of myoglobin in the muscle and the tendency to spontaneous arrest as the person affected matures) known about progressive muscular dystrophy: 1. He gave 8 patients estrogen in an effort to influence the creatine-creatinine utilization and excretion. 2. Choline, in the hydrochloric or chloride form, was given in an effort to influence the metabolism and deposition of fat. 3. An abundance of cow's or goat's milk was given in an attempt to enhance the availability of magnesium. 4. Anemia was prevented. 5. Gonadotropic substance was given in an attempt to hasten maturity and enhance the effect of the estrogen. 6. In addition, general setting-up exercises, physical therapy, fresh air and sunshine were provided. The condition of 2 of the 8 patients treated was hopeless, and they were used only to observe the effect of the estrogen. The creatinine excretion was definitely increased after treatment was started and was maintained at normal, with occasional elevations above normal. The other 6 patients were given the regimen in an effort to improve their general condition and arrest the progress of the disease. A noticeable increase in muscular strength was experienced by 3 patients, 2 were improved and at first 1 was slightly improved but had bilateral otitis media and mastoiditis and the end result was a total failure. The author points out that results over three and a half years have been so encouraging that he presents this preliminary report in the hope that other workers will try the regimen and prove or disprove its value.

New England Journal of Medicine, Boston

225:519-560 (Oct. 2) 1941

Carcinoma of Lung: Bronchoscopic Aspects. R. H. Betts, Brookline, Mass.—p. 519.
Auscultation of Heart. S. A. Levine, Boston.—p. 526.
Pollen and Mold Survey of Southwestern New England—1940. H. N. Pratt, A. Colmes, J. Fromer, J. E. Greene, Boston; F. H. Chafee, Providence, R. I., and W. B. Clapp, Worcester, Mass.—p. 533.
Physical Therapy. A. L. Watkins, Boston.—p. 539.

New Jersey Medical Society Journal, Trenton

38:495-556 (Oct.) 1941

Decline in Prevalence of Syphilis as Shown by Routine Tests in Hospital. A. J. Casselman and Anabel Cadwallader, Trenton.—p. 499.
Differential Diagnosis of Acute Lower Abdominal Lesions in Female. W. J. Carrington, Atlantic City.—p. 504.
Psychosomatic Concept in Modern Medicine. H. Wallace, New York.—p. 509.
The General Practitioner and the Electrocardiogram. J. H. Rowland, New Brunswick.—p. 513.
Epidemic Influenza. F. Hnat, Elizabeth.—p. 518.
Rheumatic Infection in Childhood. E. L. Bauer, Philadelphia.—p. 521.
Relationship Between the Medical Profession and the Hospital. E. J. Smith, Belleville.—p. 528.

Pennsylvania Medical Journal, Harrisburg

45:1-96 (Oct.) 1941

Hodgkin's Disease of Duodenum. L. C. Pusch, York.—p. 20.
Rupture of Rectus Abdominis Muscle and Associated Lesions: Collective Review and Report of Two Cases. J. C. Bulfamonte, Shamokin.—p. 22.
Surgical Treatment of Leg Length Discrepancies. P. H. Harmon, Sayre.—p. 27.
Atraumatic Surgical Suction Tube. D. J. Preston, Wilmington, Del.—p. 35.
Calcareous Tendinitis (Peritendinitis Calcarea) at Greater Trochanter of Femur. L. Kaplan, Philadelphia.—p. 37.
Management of Nose and Paranasal Sinuses in Asthma. A. T. Smith, Philadelphia.—p. 41.
*Supraventricular Tachycardia in Infancy. R. M. Keagy and R. S. Magee, Altoona.—p. 44.

Supraventricular Tachycardia in Infancy.—Keagy and Magee report that giving acetyl-β-methylcholine chloride subcutaneously terminated five attacks of supraventricular tachycardia in a boy aged 5 months. The optimal dose of the drug was 6 mg. The attack on admission was one of several which had occurred since birth, the first having occurred at 2 months. After the fourth attack in the hospital the patient was given 0.064 Gm. of digitalis twice a day in an effort to prevent further attacks. The dose was subsequently reduced until 0.008 Gm. was given daily. This proved inadequate, and a daily maintenance dose of 0.011 Gm. was decided on; the child has since had no attacks and has progressed well. An electrocardiogram taken three days after digitalis therapy was instituted shows a normal auricular and ventricular mechanism and a heart rate of 120 per minute. Although the authors feel that it is safe to use acetyl-β-methylcholine chloride they suggest that atropine be available if untoward toxic symptoms should arise. They believe that powdered digitalis leaf has been responsible for the absence of paroxysms. They say that to date there has been no substantial evidence suggesting active pathologic cardiac changes and that the diagnosis of congenital heart defect is not justifiable, although it may be suspected, as the patient has congenitally deformed ears and his sister has congenitally webbed toes.

Public Health Reports, Washington, D. C.

56:1901-1940 (Sept. 26) 1941

*Epidemic of Infectious Encephalitis. J. P. Leake.—p. 1902.
*Isolation of Western Equine Encephalomyelitis Virus from Naturally Infected Prairie Chicken. H. R. Cox, W. L. Jellison and L. E. Hughes.—p. 1905.
Eosinates of Azures and Methylene Blue in Preparation of Satisfactory Giemsa Stain from Dyes of American Manufacture. M. A. Roe, A. Wilcox and R. D. Lillie.—p. 1906.
Twenty-Four Hour Output of Certain Urinary Constituents in Persons Exposed to Lead Arsenate Spray Residue. S. H. Webster.—p. 1910.
Development of Leprous Process in Rats at Site of Inoculation with Material from Human Leprosy. G. L. Fite.—p. 1919.

Epidemic of Infectious Encephalitis.—Leake states that the largest encephalitis epidemic on record in North Dakota and bordering states and provinces has just ended. In North Dakota there were 1,080 cases with 96 deaths, an incidence of 167 per hundred thousand and a mortality of 8.9 per cent. The uniformity of symptoms and the spread of the disease throughout the area affected by the epidemic suggested that only one disease, western equine encephalitis (proved by serum-neutralizing tests), was responsible for the epidemic. In determining its spread it was found that the tremendous predominance among working men could be accounted for only by differences in exposure. Since the male population of working age has a greater exposure in the wheat fields than the female population a reservoir or reservoirs other than man or horses was looked for. Cox, Jellison and Hughes found the virus of western equine encephalitis in all animals inoculated in the spleen and the central nervous system with material isolated from the brain and the spleen of a prairie chicken, a bird of the grain fields. This indicates carriage via the blood and blood infectiousness.

Isolation of Western Equine Encephalomyelitis Virus from Prairie Chicken.—Cox and his associates believe that they are the first to report the isolation of the virus of western equine encephalitis from a prairie chicken. At the time that the bird was killed encephalitis was occurring in many human beings in the immediate vicinity of Rugby, N. D., which in fact was one of the chief foci of the epidemic.

Quarterly J. Studies on Alcohol, New Haven, Conn.

2:241-452 (Sept.) 1941

Penal and Correctional Aspects of Alcohol Problem. A. H. MacCormick, New York.—p. 241.
Neuropathologic Findings in Brain and Spinal Cord of Chronic Alcoholic Patients. L. Alexander, Boston.—p. 260.
Factors Influencing Effects of Alcohol on Blood Sugar and Liver Glycogen. D. M. Tennent, New Haven, Conn.—p. 263.
Influence of Alcohol on Emptying Time of Stomach and Absorption of Glucose. D. M Tennent, New Haven, Conn.—p. 271.
Psychogenesis of Alcoholism. P. Schilder, New York.—p. 277.
Psychiatric Resultants of Alcoholism: Alcoholism and Mental Disease. N. D. C. Lewis, New York.—p. 293.
Alcoholic Mental Disorders. K. M. Bowman, New York, and E. M. Jellinek, New Haven, Conn.—p. 312.

Surgery, Gynecology and Obstetrics, Chicago

73:433-600 (Oct.) 1941

Chronic Pericardial Disease: Report of Twenty-Eight Cases of Constrictive Pericarditis. A. Blalock, Baltimore, and C. S. Burwell, Boston.—p. 433.
Evaluation of Incapacity Produced by Injuries of Peripheral Nerves. L. J. Pollock, Chicago.—p. 462.
*Diagnosis of Chronic Enlargement of Leg, with Description of New Syndrome. J. C. Luke, Montreal, Canada.—p. 472.
Theca Cell Tumors (Thecoma). A. H. Curtis, Chicago.—p. 481.
Operation for Cure of Congenital Atresia of Esophagus. B. N. Carter, Cincinnati.—p. 485.
*Study of Platelet Count and Coagulation Time of Plasma and Whole Blood Following Operation. W. J. Potts and Elisabeth Pearl, Oak Park, Ill.—p. 492.
Oxygen Therapy in Shock Due to Hemorrhage. J. G. Schnedorf and T. G. Orr, Kansas City, Kan.—p. 495.
*Uterine Contractions of Early Pregnancy and Their Relation to Duration of Labor: Study of 250 Patients Made with Lóránd Tocograph. D. P. Murphy, Philadelphia.—p. 498.
*Liver Insufficiency in Toxic Goiter and Its Treatment. C. R. Schmidt, W. S. Walsh and V. E. Chesky, Halstead, Kan.—p. 502.
Total Cystectomy Combined with Panhysterectomy. S. A. Vest and H. H. Curd, Charlottesville, Va.—p. 517.
End Results of Treatment of Malignant Tumors of Palate. G. B. New and O. E. Hallberg, Rochester, Minn.—p. 520.
Intraspinal Epidermoids, Dermoids and Dermal Sinuses. C. F. List, Ann Arbor, Mich.—p. 525.
Appendicular Obstruction: Its Clinical and Pathologic Aspects. J. J. McCallig, Rochester, Minn.—p. 539.
Sex Hormone Excretion of Adult Female and Pregnant Monkeys. R. I. Dorfman and G. Van Wagenen, New Haven, Conn.—p. 545.
Cecostomy. A. W. Allen and C. E. Welch, Boston.—p. 549.

Diagnosis of Chronic Enlargement of Leg.—Luke discusses the numerous causes for the development of an enlarged leg and lists them under six headings: congenital hypertrophy, congenital and acquired lymphatic stasis and obstruction, developmental venous retardation, mixed venous and lymphatic partial obstruction, congenital arteriovenous fistulas and miscellaneous causes. As far as he knows, pure venous retardation as a cause of the condition has not been described. This increased size in a previously unaffected leg is not the same as that due to lymphaticovenous obstruction, in which there is also partial lymphatic blockage. A case is presented which demonstrates that venous retardation can of itself cause enlargement of a leg. The patient had no previous disorder of a leg, phlebitis, pregnancy or any severe illness. The enlargement appeared gradually in early adult life, at a time when defective venous valves in the saphenous system usually appear. Edema as a factor in the enlargement can be ruled out by the absence of pitting on pressure and only a slight diminution in size on prolonged elevation of the leg. Signs of a congenital arteriovenous fistula were not present. The diffuse cyanosis of the leg, most severe on standing, indicated venous congestion, and the absence of enlarged superficial veins ruled out incompetence of the saphenous system; however, this may develop later. Roentgen studies corroborated the clinical impression, in that the absence of valves or defective valves in the deep system of the involved leg were revealed allowing complete retrograde flow. This defect is absent in the normal leg. The hypertrophy of the leg probably resulted from the venous retardation and the prolonged activity of an increased venous pressure over a dilated deep venous bed. The extremity has undoubtedly been endowed with congenitally weaker and fewer valves than the normal leg, and the patient's years of activity as a waitress caused complete defectiveness.

Blood Platelet Count and Coagulation Time.—Potts and Pearl determined the coagulation time of the plasma, with and without platelets, of 52 patients after major operations. The coagulation time of whole blood was also studied. Estimations were made before operation and every day or every other day after operation until the patient's discharge. The average preoperative platelet count was 275,000 per cubic millimeter; on the first postoperative day it fell to 260,000 and remained so until the third postoperative day, when it began to rise so that by the fifth day it was 278,000, by the seventh 292,000 and by the tenth 301,000. By the fourteenth day it fell to 289,000 in the 24 patients who remained in the hospital this long. The average coagulation time of plasma with platelets was constantly practically the same as that of whole blood; except for a slight drop on the first postoperative day neither varied much at any time. The average coagulation time of plasma free of platelets was constantly slightly less than that of plasma containing platelets. There was no discernible relationship between the platelet count and the coagulation time. A platelet count of 120,000 was apt to be associated with a coagulation time of five minutes and a count of 400,000 with a coagulation time of ten minutes; the reverse was just as likely. It seems doubtful that the platelet count and coagulation time following major surgical procedures are of any significance in the development of postoperative thrombosis or embolism.

Uterine Contractions of Early Pregnancy.—Murphy recorded with a Lóránd tocograph the uterine contractions of 250 women between the one hundred and tenth and the two hundred and seventy-ninth day of pregnancy. No spontaneous uterine contraction was noticed until the one hundred and sixty-sixth day, and the expulsive force of contraction increased progressively during the remainder of pregnancy. Patients experiencing uterine contractions prior to the thirty-third week of gestation usually had a significantly shorter labor than those without such activity. Measurement of uterine contractions after the thirty-second week of pregnancy was of no value in predicting the type of labor to follow.

Hepatic Insufficiency in Toxic Goiter.—According to Schmidt and his associates, of 207 consecutive patients with goiter subjected to thyroidectomy 113 presented evidence of hepatic insufficiency as measured by the Quick hippuric acid test. In 34 of these patients the hippuric acid excretion was less than 70 per cent of normal. Hepatic insufficiency appeared related more to the duration and intensity of the thyrotoxicosis than to the type of goiter. Patients receiving specific measures directed at correcting hepatic function showed greater improvement and were better operative risks than a control group of patients treated only by conventional measures. Postoperative morbidity and mortality of severely toxic patients with goiter probably can be significantly decreased by therapeutic measures directed at improving hepatic function. The authors have had only 1 of 370 consecutive patients die after thyroidectomy.

Southern Surgeon, Atlanta, Ga.

10:695-772 (Oct.) 1941

Multiple Dissimilar Carcinomas of Stomach. R. L. Sanders, Memphis, Tenn.—p. 695.
Conservatism and Pelvic Inflammation. D. M. Clardy, Hopkinsville, Ky.—p. 705.
Pathology and Surgical Management of Acute Head Injury. E. S. Gurdjian, Detroit.—p. 711.
Sulfanilamide in Local Treatment of Traumatic Wounds. R. O. Joplin, Louisville, Ky.—p. 733.
Role of Fascia in Low Back Pain. J. C. Pickett, Morgantown, W. Va.—p. 738.
Management of Fracture-Dislocation of Neck. C. P. Graham and J. F. Robertson, Wilmington, N. C.—p. 747.
Emergency Treatment of Burns. W. C. Tenery and J. H. Tenery, Waxahachie, Texas.—p. 759.

Southwestern Medicine, El Paso, Texas

25:275-310 (Sept.) 1941

Treatment of Nerve Injuries of Upper Extremities. R. M. Stuck, Denver.—p. 275.
Relationship of Surgical Immobilization of Both Osseous and Pulmonary Tuberculosis. F. H. Albee, Venice, Fla.—p. 280.
Recent Developments in Treatment of Urinary Infections. H. F. Helmholz, Rochester, Minn.—p. 286.
Flocculation Tests for Syphilis. T. R. Reusser, E. L. Breazeale and J. F. Breazeale, Tucson, Ariz.—p. 289.
Iris Changes in Syphilis: Further Observations. J. T. Lowry, Alamogordo, N. M.—p. 290.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:429-464 (Sept. 27) 1941

Rehabilitation of Injured Air Crews. R. N. Houlding.—p. 429.
Treatment of Hemorrhagic Disease of Newborn. A. I. S. Macpherson. —p. 433.
*Causes Underlying Recent Increased Incidence of and Mortality from Tuberculosis in Glasgow. S. Laidlaw and D. Macfarlane.—p. 436.
Avoidable Disability Seen in Recent Amputations. W. R. D. Mitchell. —p. 437.
Unilateral Clubbing of Fingers: Case with Summary of Literature. R. E. Rodgers—p. 439.
Procedure for Treatment of Gas Casualties. L. A. Stocken and R. H. S. Thompson.—p. 448.

Causes for Increased Tuberculosis Mortality in Glasgow.—According to Laidlaw and Macfarlane, for five years preceding the outbreak of the present war the incidence of and the mortality from pulmonary tuberculosis tended to stabilize themselves in Glasgow at annual figures of around 1,650 notifications and 960 deaths. During the first year of the war the returns were 1,908 and 1,177, respectively. This increase is being maintained during 1941. The increased incidence has taken place almost entirely between the ages of 15 and 45 in males and 15 and 35 in females. The figures for nonpulmonary tuberculosis for 1939 and 1940 also show a considerable rise in notifications and deaths. The possible reasons for the increased incidence are increased virulence of the tubercle bacillus, malnutrition and deficient diet, tubercle bacilli in milk, examination by military medical boards, exertion or strain of army life, long hours in shelters, overcrowding in factories and longer working hours, strain and curtailed rest. A study of these factors shows that a combination of long hours, overtime, strain and ill spent leisure has produced the rise in the number of cases of tuberculosis. The increase will be maintained while these factors remain unchanged.

Journal of Laryngology and Otology, London

56:225-276 (July) 1941

Protection of Hearing. E. D. D. Dickson and A. W. G. Ewing. —p. 225.
Tonsillectomy in Child with Thymic Enlargement. R. G. Macbeth. —p. 243.

Journal of Neurology and Psychiatry, London

4:97-162 (April) 1941

Alzheimer's Disease with Predominating Crossed Cerebrocerebellar Hemiatrophy. R. E. Hemphill and E. Stengel.—p. 97.
*Electroencephalogram in Acute Head Injuries. D. Williams.—p. 107.
*Electroencephalogram in Chronic Post-Traumatic States. D. Williams. —p. 131.

Electroencephalogram in Acute Head Injuries.—Williams made electroencephalograms of 74 patients (drawn from a series of 600 patients admitted to a special center for injuries of the head) within twenty days of their injury. The initial electroencephalograms of 42 of the 74 patients were normal, and their subsequent clinical recovery was uneventful. The patients were unselected, and all were members of the army and the Royal Air Force. Their ages ranged from 18 to 60 years. Their injuries varied from simple concussion to severe cerebral laceration with dural penetration and cerebral herniation. Slow waves were invariably present when consciousness was impaired. The degree of abnormality was closely correlated with the clinical state of the patient. In patients with severe injuries the abnormalities persisted for many weeks. The rate of clinical and of electroencephalographic recovery corresponded closely, but there were wide individual variations in the speed of return to normal. In the later stages of recovery the electroencephalogram was sometimes abnormal after the patient had made a complete clinical recovery. Localizing clinical signs corresponded with the area of abnormality seen in the electroencephalogram. An epileptic type of disturbance occurred in the immediate post-traumatic period, but it had no prognostic significance in relation to post-traumatic epilepsy. The author concludes that the electroencephalogram accurately reflects the abnormal cerebral state caused by a recent injury to the head, that the progressive changes are a direct indication of improvement or deterioration and that in the milder instances of cerebral dysfunction it may demonstrate residual damage after abnormal clinical signs have subsided.

Electroencephalogram in Chronic Post-Traumatic States.—Williams states that the electroencephalograms of the 600 previously mentioned service personnel were taken from a few hours to twelve years after injury. Fifty per cent of the patients had abnormal electroencephalograms. This high percentage persisted for many years after injury. There was a positive correlation between it and the severity of the injury, the persistence of symptoms and dural penetration. Of 87 patients invalided from the services, 67 per cent had an abnormal electroencephalogram. In 207 patients, 55 per cent of whom had abnormal electroencephalograms, the symptoms were thought to be due to organic damage. The electroencephalograms of 37 per cent of 50 constitutionally inferior patients and of 20 per cent of 58 with symptoms due to an exogenous neurosis were abnormal.

Lancet, London

2:359-386 (Sept. 27) 1941

Home Guard Medical Arrangements. A. L. Abel.—p. 359.
*Middle Class Diets in Peace and War. E. M. Widdowson and B. K. Alington.—p. 361.
Sneezing in Spread of Infection. R. B. Bourdillon and O. M. Lidwell.—p. 365.
Corrosive Stricture of Stomach Without Involvement of Esophagus. C. A. R. Schulenburg.—p. 367.

Middle Class Diets in Peace and War.—From a study of the records of a dietary survey made in 1935 on 63 men and 63 women of the English middle class Widdowson and Alington found that in 1935 the men ate an average of twice as much sugar and bacon, three times as much meat, butter and jam and five times as much cheese as rationing allowed them in the spring of 1941. In 1935 the women ate less of these foods than the men, but the quantities, with the exception of sugar, exceeded the rationing in the spring of 1941. A survey of the diets of 57 middle class women in the spring of 1941 revealed that much less raw fruit and less unrationed meat, fish and sweets were consumed by the women than in 1935. However, milk, bread, cereal foods, potatoes and vegetables were being consumed in larger amounts in 1941. The 1941 survey showed that a prewar level of calories was maintained by the women by substituting unrationed carbohydrate for rationed fat. Their intake of protein, other than animal protein, and of phosphorus was unchanged, and their calcium and iron intake was higher in 1941. The average daily vitamin C intake in 1935 was 57 mg. and in 1941 it was 27 mg. The decrease was due to the unavailability of raw fruit.

Medical Journal of Australia, Sydney

2:311-342 (Sept. 20) 1941

Treatment of Thyrotoxicosis. S. A. Smith.—p. 311.
Surgeon's Responsibilities in Thyrotoxicosis. H. R. G. Poate.—p. 313.
Radiotherapy in Thyrotoxicosis. C. de Monchaux.—p. 316.
Technic of Subfascial Thyroidectomy. H. R. G. Poate.—p. 318.
Adrenal Cortex. A. B. Corkill.—p. 324.

2:343-374 (Sept. 27) 1941

Hemorrhage, Anemia and Jaundice in Newborn. F. Arden.—p. 343.
Nutritional Anemia in Infancy: Review of 277 Sydney Infants at Age of Nine Months. N. C. Cunningham.—p. 349.

2:375-404 (Oct. 4) 1941

Prevention of War Neuroses. W. S. Dawson.—p. 375.
Psychiatric Practice and Clinical Medicine. N. V. Youngman.—p. 378.
Causation of Fractures of Neck of Femur. E. Sandner and E. C. Thompson.—p. 383.
Aminoplastin in Abdominal Surgery. F. A. Maguire and A. R. Scott-Orr.—p. 391.

Practitioner, London

147:545-608 (Sept.) 1941

Septicemia and Allied Conditions. T. B. Davie.—p. 545.
Medical Aspects of Septicemia. C. E. Lakin.—p. 553.
Surgical Aspects of Septicemia. R. J. M. Love.—p. 559.
Puerperal Septicemia. R. M. Corbet.—p. 565
First Aid in Wounds and Hemorrhage. A. C. W. Knox.—p. 572.
First Aid in Asphyxia. M. M. Scott.—p. 580
First Aid Treatment of Injuries of Eye. W. J. W. Ferguson.—p. 589.
Minor Surgery: III. Minor Surgery of Hand. N. C. Lake.—p. 593.

Archivos Argentinos de Tisiología, Buenos Aires

17:177-270 (April-June) 1941. **Partial Index**

Amount of Water Vapor Expired in Eupnea and Its Determination in Relation to Clinical Work on Tuberculosis. A. Raimondi and A. S. J. Pena.—p. 177.
Tuberculosis of Mixed Localization. O. P. Aguilar, G. Sirlin and J. Queirel.—p. 189.
*Hemorrhagic Pleurisy and Hemopneumothorax. A. A. Raimondi and S. Lerner.—p. 215.
*Results of Roentgenologic Examination of Attendants of Tuberculous Patients. A. Raimondi, Jr.—p. 227.
Bilateral Phrenic Exclusion. O. P. Aguilar and C. A. Bancalari. —p. 235.

Hemorrhagic Pleurisy and Hemopneumothorax.—Raimondi and Lerner define those pleural effusions which are red and contain a large number of erythrocytes as hemorrhagic pleurisy. Although the most important causes are cancer and tuberculosis, hemorrhagic pleurisy can be found also in acute rheumatism, typhoid, pneumonia, influenza, syphilis, hepatic cirrhosis, nephritis, malaria, chronic alcoholism and hemorrhagic disorders, such as scurvy, purpura, leukemia and smallpox. The pathologic aspects of hemorrhagic pleurisy are similar to those of serofibrinous pleurisy, with the difference that one frequently encounters abundant proliferation of new vessels and pleural membranes. The increased number of erythrocytes in the effusion is due to such mechanisms as diapedesis and rupture of newly formed capillaries and of fragile walls. The effusion is bright red, but if old it takes on a violet color. Cancer is the cause so frequently that whenever hemorrhagic pleurisy exists it is necessary to employ all diagnostic aids that will eliminate cancer as a possible cause. Hemorrhagic pleurisy can supervene in patients with cancer of the stomach, the uterus, the breast and so on, and it may indicate that metastasis has taken place. When it is the first sign of cancer, two possibilities must be considered: (1) that hemorrhagic pleurisy may mask a tumor which, after the evacuating puncture, can be easily recognized clinically by various forms of roentgen examination and bronchoscopy; (2) that hemorrhagic pleurisy may be symptomatic of primary cancer of the lung or the pleura, in which case the clinical difficulties are great. Tuberculosis is the other frequent cause of hemorrhagic pleurisy. It may be primary or secondary to acute or chronic pulmonary tuberculosis. In order to characterize hemorrhagic pleurisy as tuberculous and primary, the following conditions must be fulfilled: (1) absence of tuberculous lesions, (2) presence of tubercle bacilli and (3) appearance of tuberculous lesions immediately after production of the effusion. On the basis of these conditions primary tuberculous hemorrhagic pleurisy is extremely rare. Secondary tuberculous hemorrhagic pleurisy is more frequent than the primary form. It may occur in acute forms (miliary tuberculosis, caseous tuberculosis) or in chronic forms. When accompanying the acute forms, it is frequently bilateral and characterized by intense dyspnea and a rapidly fatal evolution. When secondary to chronic pulmonary tuberculosis, the development is determined by the pulmonary status. Hemorrhagic pleurisy may supervene after suspension of artificial pneumothorax. If it takes a benign course, the treatment consists in the evacuation of the effusion with or without reinsufflation of air. The malignant form, which is less frequent than the benign, is produced when a subpleural tuberculous lesion opens into the pleural cavity. In this condition, thoracoplasty seems to be the only therapy likely to prevent a fatal outcome. Discussing spontaneous hemopneumothorax, the authors show that hemorrhagic pleurisy is customarily not an inflammatory condition but a hemorrhage accompanying spontaneous pneumothorax. Both the tuberculous and the nontuberculous forms of spontaneous hemopneumothorax are rare. They encountered only 3 cases in 94,914 case records.

Roentgenologic Examination of Attendants of Tuberculous Patients.—Raimondi made periodic roentgen examinations of 371 persons who lived in an environment where they were exposed to tubercle bacilli and found that 21 per cent had mild or grave forms of tuberculosis. The majority began with a form of tuberculosis that presented no symptoms or only slight symptoms. The incipient lesions are tractable to treatment; success is often obtained with ambulatory treatment. It is essential to convince persons who live in the environment of patients with open pulmonary tuberculosis of the necessity of periodic roentgenologic examinations, because, although subjective symptoms may be absent, pulmonary lesions may at times advance unnoticed. Periodic examination will insure diagnosis when the disease is in the incipient phase, so that it will be possible to institute effective treatment. The author calls attention to the relative frequency with which hematogenic forms are encountered in adolescents and young adults who are exposed to infection. On the basis of statistical studies and of several observations the author supposes that exogenic reinfection is of importance in the genesis of the disease.

Tokyo Igakkwai Zassi, Tokyo

55:529-620 (July) 1941. **Partial Index**

*Histopathologic Studies of Diabetic Kidneys with Special Reference to Changes in the Glomeruli. R. Murakami.—p. 529.

Glomerular Pathology in Diabetes.—Murakami made histologic studies of kidneys in 27 cases of diabetes mellitus, including 7 instances of death resulting from acidotic coma, with special reference to the changes demonstrable in the glomeruli. The most striking changes in diabetic kidneys were found to be enlargement of the glomeruli due to both regressive cellular swelling of the basement membrane and progressive hypertrophy and hyperplasia accompanied by hyperemia. Hyalinization, fibrotic union of capsules and fatty and glycogen degeneration of the parenchyma were also noted. All these changes in some instances at least appeared to be reversible, paralleling the clinical course in each case, but parenchymatous degeneration was not clearly demonstrable in cases of acidotic coma or of renal complications. Although the pathologic changes of the diabetic kidney resemble those seen in nephrosclerosis, the two conditions can be cytologically differentiated. The changes may be regarded as a cumulative product which is compensatory to functional disturbances, caused by the stimulating effect of overfunctioning organs and of tissues saturated with the abnormal composition of the urine. The predominance of these changes occurring in the glomeruli and the terminal capillaries may be due to the chief excretory function which these tissues perform, together with the contributory effect of the specialized structure of the glomerular tufts. The appearance of epithelial cells at the end of the Bowman capsule is probably but an extension of the main epithelium. Although there is no direct evidence of any organic relation between this disease and other lipemic diseases, yet the abnormal enlargement of the glomerular tufts may aggravate the lipemic kidney and accentuate the existence of such diseases by epithelial hypertrophy. The diabetic kidney may thus be regarded as representing a case of glyconephrosis under the general category of glomerular nephrosis.

Ugeskrift for Læger, Copenhagen

103:1201-1230 (Sept. 18) 1941

Advances in Operative Treatment of Recent and Older Fractures of Neck of Femur, Especially Personal Experiences with Lindén's Percutaneous Method. K. Lehmann.—p. 1201.
Conditions Concerning Abdominal Rigidity, Especially in Acute Appendicitis. O. Raagaard.—p. 1208.
*Changes in Visceral Blood Vessels in Thromboangiitis Obliterans (Buerger). G. Teilum.—p. 1211.
Dyscraniodysphalangia: Case. T. Grinsted.—p. 1215.
Treatment of Scabies with Dixanthogén Petrolatum. H. Haxthausen. —p. 1217.
Cases of Hemorrhage in Peritonsillary Abscess. T. Krarup.—p. 1219.

Visceral Blood Vessels in Thromboangiitis Obliterans.—Teilum reports a case of severe thromboangiitis obliterans in a man aged 43 with gangrene of both lower extremities. Necropsy showed, besides the characteristic changes in the arteries of the extremities and of the pelvis, (1) thickening of the intima and obliteration of the peripheral part of the main descending branch of the coronary artery, with corresponding myofibrosis, and (2) a juxtapyloric ulcer in the stomach with thickening of the intima and more peripherally almost complete obliteration of the afferent arterial branch. This, together with a few similar observations previously published, supports the assumption that in Buerger's disease there is a general disturbance of the arterial system.

THE STUDENT SECTION

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The Future of Pediatrics

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Although pediatrics is one of the oldest of the clinical specialties, dating from Bagellardus, Metlinger, Phaer, Hieronymus, Sainte Marthe and Glisson (1453-1600),[1] it is only in recent years that the growth has been rapid, owing in no small part to a demand on the part of the public for better medical care for the child.[2] This same demand is leading to more intensive development of child health activities on the part of the state and to the acceptance of the ideas that the health of the child is a responsibility of the government somewhat analogous to the way in which education has been a state responsibility and that, if the American child is entitled to an education, he is entitled to health.[2] At present pediatrics, through its own commendable efforts in prevention [3] and also for economic reasons, may lose its strictly clinical aspect and become increasingly merged with preventive medicine and public health. In fact, the pediatrician is fast becoming a liaison officer between the public health service and private medicine.[4]

There are four reasons for this trend: (1) the advances in preventive pediatrics, (2) the nature of pediatric practice, (3) the increasing number of pediatricians and (4) the improved pediatric training of general practitioners.

1. The advances in preventive pediatrics, most of them made by pediatricians themselves, have eliminated many of the pediatric problems, so that the need for practicing pediatricians is decreasing. A generation ago the majority of patients were children. Now ill children are in the minority because (*a*) diphtheria, whooping cough, dysentery and typhoid are becoming rarities, (*b*) pneumonia, meningitis and dysentery are successfully treated with sulfonamide derivatives, (*c*) congenital syphilis is reduced through more adequate treatment of pregnant women, (*d*) infant feeding is simplified [5] and nutritional knowledge increased, (*e*) the mortality in children has decreased 66 per cent and (*f*) the ratio of children to the total population is reduced from 1:3 to 1:4 as the result of the falling birth rate and the increased longevity of adults.[6] However, the need for continued and improved preventive pediatrics cannot be overemphasized; 75 per cent of the deaths among children are preventable, and it is in this field, as well as in practice, that pediatricians always will be needed. More and better research on the cause, cure and prevention of children's diseases, in addition to greater stress on preventive pediatrics, also is necessary.

2. Pediatrics is essentially general practice limited to the care of children from birth or even before birth to or through adolescence [7] and therefore pediatricians are in constant competition with other specialists, health and infant welfare agencies and with general practitioners, for "the majority of the children in this country are cared for by general practitioners and not by pediatricians." [8] Furthermore, the percentage of graduates who are going into general practice apparently is increasing.

3. At present there are 4,205 pediatricians—2,205 full specialists and approximately 2,000 partial specialists—of whom 1,620 have been certified by the American Board of Pediatrics.[9] It is possible that the opportunity for successful pediatric private practice may be lost because of a supply greater than the demand.[2] It is doubtful whether the public can support a larger

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital.

Read before the eighty-seventh meeting of the Medical Society of the State of North Carolina, Pinehurst, N. C., May 15, 1940.

1. Ruhräh, John: Pediatrics of the Past, New York, Paul B. Hoeber, 1925; Davison, W. C.: The Future of American Pediatrics, J. Pediat. **14**:810-814 (June) 1939.

2. Veeder, B. S.: The Position of Pediatrics in the Present Day Practice of Medicine, Pennsylvania M. J. **44**:1233-1239 (July) 1941.

3. Davison, W. C.: Preventive Pediatrics, J. A. M. A. **114**: 742-746 (March 2) 1940.

4. Evans, C. A.: What Has Pediatrics to Offer? Medical Economics **18**: 40-44, 92-98 (May) 1941.

5. Student song on simplified feeding with evaporated milk:

"No teats to pull,
No dung to fling,
Just punch two holes
In the Goddam thing."

6. Davison, W. C.: Opportunities in the Practice of Medicine, J. A. M. A. **115**: 2227-2232 (Dec. 21) 1940. Veeder.[2]

7. Davison, W. C.: Pediatrics: What Is It? J. Pediat. **3**: 64-77 (July) 1933.

8. Council on Medical Education and Hospitals of the American Medical Association: Medical Education in the United States, 1934-1939, Chicago, American Medical Association, 1940.

9. Veeder.[2] Evans.[4]

number of pediatricians, as half of the babies born each year are in families on relief or with an annual income of less than $1,000. Fair remuneration to the physician is essential to good care.[2] As the average age of the practicing pediatrician is approximately forty years and replacements will be slow, graduates of today who wish to care for children may have difficulty as specialists and probably should enter general practice or obtain health department positions, even though this statement may be interpreted as a lamentation of Jeremiah or a tribulation of Job.

4. The improved teaching of pediatrics in the medical schools has enabled many of the present graduates who are going into general practice to have a more practical knowledge of pediatrics than some of the interns in the children's hospitals had a generation ago.[2] In addition, the increased number of pediatric internships has made postgraduate pediatric training available for general practitioners. Twenty years ago almost all pediatric interns went into pediatric practice, but during the past ten years 40 per cent of those at Duke Hospital have gone into other fields.

In spite of these trends in pediatrics, some practicing pediatricians always will be needed, as the clinical problems of children differ from those of adults.[10] Pediatric teachers and members of state and federal health organizations also are necessary in order to perpetuate and increase the advances made in preventive pediatrics.[3] Most of the present American pediatricians are maintaining successful practices, particularly those who emphasize preventive measures and include child guidance, mental hygiene and adolescent care in their field.[11] The small to medium sized cities are the best places in which to practice, as the larger cities are oversupplied with specialists and the small towns can seldom support them. Low fees for prophylactic measures, which are given free by health departments, and agreements with a family to render pediatric services for an annual fee have been helpful, i. e. full service of unlimited office and home visits and immunization for $60 to $85, or well baby service of office visits and telephone calls but not home visits for $35 to $80.

The problem of pediatric instruction in medical schools has therefore changed; in 1930 it consisted in teaching pediatrics to medical students, most of whom planned to enter some specialty, and the provision of postgraduate training, through internships and residencies, for future pediatricians. Now the latter are decreasing, but a greater need has arisen—the laying of a sound foundation for every student's development in pediatrics, especially in the care of newborn infants, as 40 per cent or more may go into general practice, and short intensive pediatric courses for physicians who have been in general practice for several years. Duke University's answers to these new demands are a heavy pediatric teaching schedule (two hundred and seventy-nine hours), pediatric internships and residencies, obstetric-pediatric internships and weekly obstetric-pediatric postgraduate courses for general practitioners, sponsored by the North Carolina State Board of Health, the U. S. Children's Bureau and the University of North Carolina School of Public Health.

10. Sweet, Clifford: Opportunities in Pediatric Practice, J. A. M. A. **111**: 893-897 (Sept. 3) 1938. Veeder.[3]

11. Casparis, Horton R.: Some of the Preventive Aspects of the Mental Health Problem, J. A. M. A. **106**: 2207-2209 (June 27) 1936.

Digests and Reviews

PERSONALITY IN PRACTICE

Abbreviation of an address to the graduating class by Dr. Louis J. Karnosh, of Western Reserve University School of Medicine, Cleveland, June 11, 1941, published in the Clinical Bulletin of that school in September.

What you have achieved today places you in in a unique category which you will more keenly appreciate through experience. An analysis of the bibliographic indexes published in this country reveals that the probabilities of your becoming distinguished by virtue of being a physician are five times as good as they are for a lay or nonprofessional person. This implies great expectations, but by the same token it also implies that a stark failure among you is all the more glaring.

Despite the fact that you are now marked men and women, the distinction you are acquiring today is in a sense an artefact. The class of 1941 remains as a vertical sampling of normal human nature. The degree of Doctor of Medicine does not restratify, neither does it stereotype your individual personalities. The same proclivities and dispositions which were in part displayed in your freshman aptitude test, which were exposed as the unguarded mannerisms of the classroom and which more freely exude from you in the informal atmosphere of the fraternity house or dormitory, will still guide and propel you in definite directions. These make for the prime differences which exist among physicians—no more, no less than they do among stock brokers or laborers or members of the Thursday lunch club.

A SORT OF INTELLECTUAL FANATICISM

I should like to speak of virtues which, because they are virtues, may be allowed to grow on one to the point of becoming unbecoming and disabling. I shall speak first of those among you who are the factualists and precisionists in medicine. You represent the heart of medicine, without which there can be no supporting frame or structure. Your ultimate criterion is the test tube, your senses are tuned to a cold objectivity, and the ailing body is a synthetic mass of malfunctioning organs. In your tower of crisp calculations you make invaluable deductions, but your precisionism is sometimes acquired at the cost of an appropriate sense of humor. Patient with all other facts in medicine, you may find yourself impatient with the fact that the ailing person stubbornly insists on being emotional and sentimental. You can't count on him as you can on the Bence Jones protein reaction. Cold objectivity has its place in the ivory tower, but at the bedside it may become a piece of clumsy grotesqueness. The distinction between a human being and a guinea pig becomes wider and wider the more remote in recollection become your experimentations in the laboratories of the medical school.

The pursuit of a specific item by a method of precision and the feverish desire to apply it to the humanities may often become a sort of intellectual fanaticism. This is well demonstrated in the case of Bischoff, one of the leading anatomists of Europe, who thrived some seventy years ago. He carefully measured brain weights, and after many years' accumulation of much data he observed that the average weight of man's brain was 1,350 Gm., that of a woman only 1,250 Gm. This at once, he argued, was infallible proof of the mental superiority of men over women. Throughout his life he defended this hypothesis with the conviction of a zealot. Being the true scientist, he specified in his will that his own brain be added to his impressive collection. The postmortem examination elicited the interesting fact that his own brain weighed only 1,245 Gm.

It is well to develop the hard sheen of scientific exactness in the laboratory; it is just as important that in the clinic and the sickroom this surface be polished to a softened and velvety patina. The addict to exactness must be frequently reminded that in the art of medicine a sick patient who gets well without a diagnosis is better off than a dead one with a complete pathologic report.

Second, there is the classmate among you with the encyclopedic mind. It is often announced by a jeweled display athwart the vest buttons. You are hailed as a ready reference system which forestalls the need of frequent visits to the library—in short, a walking bibliography. Of you we can never be too proud, provided all your other sensitivities are equally astute, especially the nerve endings in your finger tips, and provided your lingual muscles are not overexercised at the expense of those in the forearm and hand. Yet, if you are so blessed, your virtues are tempered by certain unfavorable drifts. Pedantry and peripatetism are your trends, which is another way of saying that at times you may become an awful bore.

There is a temptation on the part of the encyclopedic medical mind to feed too much on the rarities and unique syndromes. It is above the common cold and simple constipation. It should live on simpler fare. It is too fond of wandering into obscure entities and diverticula, where it loses itself in a maze of didactics. This often exposes it to ideas and medical vogues which are new but not true; a reputation built up by exploiting them may go up with the rocket but may also come down with the stick. The encyclopedic mind holds too many "dry clinics" which soon develop into sterile husks of medical thinking and reasoning. Hold more steadily to the homely values of simple judgment and practical insight if you are encyclopedic. Resist the temptation to dysintellectualism, refrain from looking down your intellectual nose; avoid picayune argument; avoid the tendency to show the supercilious stance and to accuse dissenters of "intellectual dishonesty." This is a self rationalization which may degenerate into a cheap and pathetic pose.

We now come to a third and most familiar proclivity—the classmate who by the grace of God and not by reason of having taken a course in psychobiology is endowed with a ductile ease in getting along with people. If you are so gifted, you are blessed with a rich intuitive knowledge of human nature and a reflex-like facility in saying the appropriate thing at an appropriate time. So potent are these values that they have made some men of medicine demigods. But let them not be matched grain for grain by an equal weight of factual knowledge and they develop fatal toxic properties, making of men conceited fools and dangerous buffoons.

If you are of this ilk, a loose empiricism in practice is your greatest temptation. It's so deadly easy to rely on the oily word and the light touch of a solicitous hand, to bank on too much intuition. So easy to gravitate without too much strain of the conscience into that dangerous borderland between a flimsy empiricism and a frank charlatanry. Less excusable is your position than that of the quack, for unlike you he cannot conceal his lechery behind the robes of legitimate medicine.

A HAPPY BLEND OF HUMAN INGREDIENTS

Over in the corner and probably in the back row, unless you are alphabetically arranged, is the modest, level, plodding member of the class, who is perhaps a little lusterless but who studies quietly and passes his courses without fanfare or scintillation. His tempo, perhaps, is a little slow but it is steady. There are no spurts of brilliance, neither are there demonstrations of failure. Call him average, if you will, or even worse: he will continue his even mien through a prescribed routine. In some quiet by-way or in a village street you will shortly see his name plate. Not enough has been written about the average man. Pray, where would be the brilliance and erudition of great clinicians and teachers if these could not be contrasted against a somber setting of substantial, average men who practice medicine in an average town in an average way? Take heart, if the world stamps you as average, for if your virtues are not strongly positive then it follows that your weaknesses are likewise bland and forgivable.

In substance I do not believe that the class of 1941 possesses some of the startling hybrids I have just described. Yet these trends are there to some degree. I know that you are a happy blend of human ingredients wherein every good attribute is made stronger by reason of its constant tension with an undesirable one. Like carbon in steel, your weaknesses will give tensile strength to character.

If you truly believe that here, today, you begin to be what you are to be forever, how absorbing and fascinating will be your prospects! Give the lie to the claim that physicians so drug themselves with the routine of the sickroom that they become inarticulate in the drawing room. Conversation is a traffic and, if you enter it without some stock of knowledge, the trade drops off. To obtain knowledge, one must read. The physician, if his reading time is restricted, should by preference read the newest works in science, in literature the oldest. New books revive and redecorate old ideas; old books suggest and invigorate new ideas.

INCENTIVES AND REWARDS

Money, gratitude and technical success cannot be your only awards. Education, philanthropy and industry are deeply tinctured by medical analogies and medical ideals. The newspapers are full of medical items and articles. Almost any medical book can get itself published. It is fair to say that no other profession excites today so large a measure of public interest in all classes. On this wave of public interest the medical profession is riding either for good or for evil result. To keep medicine in fashion it must continue to merit the public sympathy and approval. We charge you to strengthen your resolves and sharpen your wits to keep it so.

INTERN LABORATORY EDUCATION IN THE GENERAL HOSPITAL

Condensation of a paper by Herman H. Van Horn, M.D., published in the Pennsylvania Medical Journal, November 1941, page 136.

The intern who comes to us in July for one year of postgraduate work is not a usual person. He is one of six thousand a year from a population of one hundred and forty million. He has an unusual background. He is a product of one of the most high pressured educational institutions in the world—the American medical school. For eight years since high school he has been in training, his instructors have included leading men of the country in medicine and surgery and, incidentally, his expense has amounted to several thousand dollars.

Moreover, this postgraduate student has a historical background as striking as any other portion of all educational history. In the last quarter of the nineteenth century microbiology was born and modern medicine became a fact. Laboratories, microscopes and full time instructors became essential factors in the modern advance. Then from 1900 to 1910 a cyclone of reformation struck the medical schools of this country, and those which survived began a remarkable metamorphosis into the powerful educational units that they are today. Also in that first decade of this century came the Council on Medical Education and Hospitals, which in 1904 inaugurated the intern year in the general hospital. Thus the general hospital was drawn into the picture, and to it was added an educational function. Today, if a general hospital is fortunate enough to be on the relatively small approved list of teaching hospitals, a large and definite educational responsibility is placed on its doorstep each year in July when the interns arrive. The nature of this responsibility has been well analyzed in THE JOURNAL by Nathan Smith and placed squarely where it belongs—on the shoulders of two groups: (1) the hospital administrators and (2) the members of the staff.

I can speak only for the course in laboratory education. I believe that it is well at the beginning of the year to file with the superintendent a written outline of what I hope to teach the intern and how I expect to do it. This is of interest to the superintendent and also tends to clear the matter in my own mind.

The aim of this course is to produce a physician so trained by his eight weeks in the laboratory as to be truly skilful in the laboratory part of his diagnostic work. The aim is to avoid a gap between the future physician and the laboratory, which he will so much need at the future time. In this course he will be taught a knowledge of some forty-five fundamental tests and will do them so frequently that they

will become a part of his equipment. He will learn the value of laboratory tests in their true perspective and not expect them to take the place of history, inspection, reflection, palpation, auscultation and percussion. He will learn to order the tests which are diagnostic rather than those of slight or remote scientific interest. He will learn that orders for laboratory work should come when and only when the history and physical examination are fresh in mind and call specifically for this or that test. He will learn that negative results from laboratory work are of little value and may sometimes be ignored in the face of other evidence. He will learn to reorder at proper intervals those tests which are helping to check the clinical changes in his patient. He will also learn that laboratory tests cost some one labor, time and material, have definite economic value, and must be paid for by his patient even as his medical bill must be paid. This will deter him from unnecessary expense to his patient. He will learn to use simple tests rather than complicated ones, when just as much can be learned from them.

To work out a method to attain this high aim and do this work in eight weeks is no mean problem. After talking with other pathologists, I discovered a teaching method being worked out in 1940 by a pathologist who felt as I did and who was introducing it in a teaching hospital in New York. This method appears to me as ideal as possible for this work in this period of time. There are four points in this method:

A separate work space must be provided for the intern and adequately equipped for his procedures. This may be known as the intern laboratory. If an entire separate room is not available, a corner of some other room can be utilized and complete equipment installed. This can be done at an expense of about $400, and in 35 square feet of space. Such a laboratory can readily be created in any teaching hospital. I used a corner of a room adjoining my main laboratory. This assures the intern privacy and a chance to think. It also definitely avoids confusion in the main laboratory, where every one is busy.

We proceed in this course to give the intern during the first one of his eight weeks a working acquaintance with forty-five of the most fundamentally diagnostic tests that are done in a clinical laboratory. We ask him to bring to us on his first day in the laboratory a list of the tests which he has learned in his medical course and which he feels competent to do. This list may be short—mainly blood counts and urinalyses. This does not matter. A technologist is assigned to introduce him to his laboratory and equipment and check with him on the tests he has already done to find if his technic can be improved. He is then given a list of forty-five tests by the pathologist, who discusses these tests with him and explains more fully the nature of this course. With the aid of the technologist these tests should be done by him, some six or seven a day during the first week. There is no doubt that this will be a busy week for him and will take most of a technologist's time, but it can readily be done.

Having thus refreshed his mind as to laboratory tests and technical methods, the following seven weeks are utilized as follows: From ward patients in various services a list is selected. As far as laboratory work is concerned, these will be his own patients. The list may be made small or large but should be as large as his time will permit. All orders on these patients will be given to him as soon as received in the laboratory. He will learn to know these patients and to do and report whatever laboratory work is requested on them at any time. He may also do other tests on them if he is so inclined. Thus for seven weeks he will be correlating laboratory tests with individual patients. Findings and diagnoses as well as surgical specimens will be discussed with the pathologist, other interns and staff men in the services. This follows and continues the educational principle of correlation, which was the basis of all his various clerkships in medical school.

Beyond this main line of work covered by the preceding three points there are a variety of special procedures for which the laboratory intern will find time as the occasion arises in ward cases. He will do lumbar punctures, gastric studies, duodenal drainage, blood transfusions and studies in allergy. He will do the current autopsies, under supervision, and with special reference to routine sequential procedure and thoroughness. He will study microscopic preparations from the autopsies and will study gross and microscopic surgical specimens. He will also be asked to prepare and present specimens at clinical conferences. He also should keep a list of all the work he does each day for summarizing at the end of his course.

DO YOU KNOW WHAT PHYSICIAN—

1. Was the first physician in New England arriving on the Mayflower?
2. Was the first to practice midwifery in America on a scientific basis?
3. Was the author of the first publication on a medical subject in America?
4. Was a famous explorer?

(The answers are on page 2290.)

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

Joint Meeting of Association of Medical Students and the Intern Council of America

The Association of Medical Students and the Intern Council of America will hold their annual meeting jointly at International House, University of Chicago, December 27-29. The general theme of the meeting will be "Health and the Defense of the Nation." Among the speakers will be Drs. Morris Fishbein, Chicago, editor of THE JOURNAL; William D. Cutter, Chicago, secretary of the Council on Medical Education and Hospitals; Fred C. Zapffe, Chicago, secretary of the Association of American Medical Colleges; Victor Johnson, dean of the University of Chicago College of Medicine; Charles S. Bacon, professor emeritus of the University of Illinois College of Medicine, Chicago, and Henry Sigerist of Johns Hopkins University School of Medicine, Baltimore.

Yale Increases Elective Hours of Study

On recommendation of the committee on program and policy, Yale University School of Medicine, New Haven, Conn., has revised the curriculum by establishing a two to one ratio between required and elective hours of study, so that about eight hundred hours a year will be allotted for required work and four hundred hours for elective work. The required courses will be held in the mornings only during the first two years of study, leaving all the afternoons free for elective courses. The number of hours of required work in the medical school mounted steadily for the past ten years until the time left for elective courses was less than one hundred and sixty hours for freshman and sophomore students and no time for third year students unless they voluntarily remained in school through the summer. Dean Francis G. Blake of the school of medicine, according to the New York *Times*, said of the foregoing change that "the revision of the curriculum is a reaffirmation and a further elaboration of the liberalized educational program which was initiated at Yale in the early 1920's and based on the fact that the medical student as an adult already has embarked on his life's work and therefore must learn both to pilot his own boat and assume largely the responsibility for acquiring that content of knowledge which is necessary in charting his future professional course. Dr. Samuel C. Harvey, professor of surgery at Yale and a member of the committee on program and policy, said that the formal lecture had decreased in importance in recent years because of the abundance and excellence of printed texts and that the lecture probably should be limited to work not yet available in printed form.

University of Kansas

Lewis L. Coriell '42 has been awarded the $300 Porter Scholarship for 1941-1942 at the University of Kansas School of Medicine, Kansas City. The award is granted each year to the senior student with the leading scholastic record.——Francis O. Trotter Jr. '42 has been awarded the $100 A. Morris Ginsberg prize in medicine. This award is made annually to the student who shows the highest proficiency in the medical courses of the junior year. The medical students were the guests of the local chapter of Phi Beta Pi at the annual fall medical school party at the Ambassador Hotel, Kansas City, October 8.

Minnesota's Incus Society

At the annual initiation banquet of the Incus Society, an undergraduate medical group at the medical school of the University of Minnesota, Minneapolis, Dr. Harold S. Diehl, dean and professor of preventive medicine and public health, and Dr. John C. McKinley, professor of medicine and nervous and mental diseases, gave addresses on the proposed revision of the junior and senior curriculums. The plans of the Incus Society for the year include (1) publication of a student section of the Minnesota Medical Foundation *Bulletin*, (2) symposiums on national defense, tuberculosis and the specialties, (3) the furtherance of closer student-faculty relations.

Names of British Medical Students in American Schools

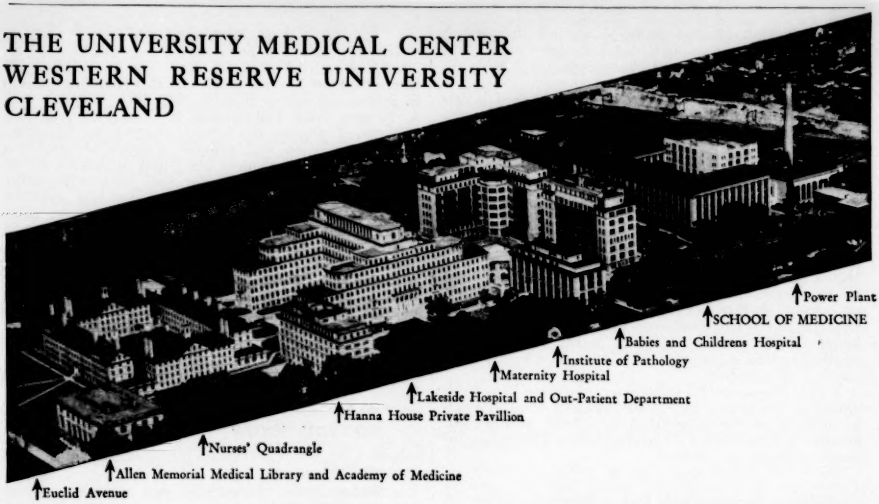
Bombing attacks on London and other cities of the British Isles have damaged medical schools and hospitals in which medical students have received their clinical training. In order to help British medical students to continue their studies, the Rockefeller Foundation has created a number of studentships which provide for tuition and other instruction fees and living costs for a period not to exceed three years. Recently twenty-five British medical students were selected from a list of about one hundred to pursue their studies in medical schools in the United States and Canada. The students were chosen by a special committee in England, of which Sir John Stopford, vice chancellor of the University of Manchester, is chairman. These students are all British citizens and expect to return to the British Isles at the termination of their training. The names of the students and the medical schools at which they are now studying follow:

NAME	SCHOOL
Badenoch, John	Cornell
Bartley, Christopher W.	McGill
Cadman, Ewan F. B.	Washington (St. Louis)
Davies, Jack	Iowa
Edwards, David A.W.	Michigan
Gibson, James B.	Western Reserve
Gosling, Robert H.	Cornell
Gray, Ian R.	Wisconsin
Hare, Patrick J.	Johns Hopkins
May, Philip R. A.	Stanford
Newton, Michael	Pennsylvania
O'Hea, Matthew A.	Washington (St. Louis)
Pond, Desmond A.	Duke
Rankine, George	Duke
Scothorne, Raymond J.	Chicago
Sharp, James	Rochester
Shephard, Reginald H.	Yale
Shepheard, John V.	Johns Hopkins
Shillingford, Jack P.	Harvard
Stephen, James D.	Minnesota
Stowers, John M.	Harvard
Swyer, Gerald I. M.	California
Tanner, James M.	Pennsylvania
Todd, Ian P.	Toronto
Turner, Robert	Yale

Georgia Student Council

The Faculty-Student Council of the University of Georgia School of Medicine, Augusta, held its first meeting of the year, November 17, at the home of the dean, Dr. G. Lombard Kelly. It was reported that the hospitalization insurance plan instituted at the school last year had proved successful so far, the individual charge of $2.50 taking care of all student hospital bills and leaving a small surplus.

THE UNIVERSITY MEDICAL CENTER WESTERN RESERVE UNIVERSITY CLEVELAND



Western Reserve University

Western Reserve University School of Medicine, Cleveland, controls for teaching and investigation purposes the clinical material of several hospitals whose bed capacity totals 2,600 and whose dispensaries are attended by 40,000 persons a year. The number of medical students at Western Reserve at present is 294. The school has graduated a total of 3,799 students "in course" and the schools which were consolidated with it graduated 1,218 students. The school of medicine of Western Reserve University was organized in 1843 as the Cleveland Medical College in cooperation with Western Reserve College; it is supported largely by endowment and special contributions, the income from tuition and fees covering but a minor part of the current budget. When the developments of medical science made the old building inadequate and accentuated the importance of close proximity to the other departments of the university, there evolved the conception of a university medical center, situated on the university campus and including not only the school of medicine with a group of university hospitals and clinics but the schools of the allied professions of nursing, pharmacy, dentistry and applied social sciences. In 1915 about 20 acres of land was secured for the medical center and since then the various buildings illustrated have from time to time been erected. While Mr. Samuel Mather and the General Education Board of the Rockefeller Foundation made magnificent contributions, it is interesting that many of the new buildings in the medical center were provided for by public subscription.

Effective July 1, 1940 the Lakeside Hospital, the Babies and Children's Hospital and the Maternity Hospital consolidated as University Hospitals of Cleveland. While the Rainbow Hospital for Crippled and Convalescent Children remains a separate institution, it also is operated by University Hospitals. In addition to the hospitals in the medical center, the university has control of the clinic material at the fifteen hundred bed Cleveland City Hospital, at the three hundred bed St. Vincent Charity Hospital and at the Ohio State Hospital for the Insane in Garfield Heights.

Western Reserve University School of Medicine is now the legal successor to all the regular medical schools that have existed from time to time in Cleveland, including the medical department of Wooster University, the medical department of Ohio Wesleyan University and Charity Hospital Medical College. Admission to the school is restricted so that the number of students in the upper classes ordinarily will not much exceed sixty. The total necessary expense, exclusive of tuition and fees but covering books and instruments, board and room, for thirty-four weeks need not, according to the official bulletin of the school, exceed $600. The outlay for clothing, traveling expenses and incidentals depends on the student. A deposit of $100, one fifth of the tuition of the first year, must be made by the applicant when he definitely accepts a place in the school, and this deposit is applied to the first payment on tuition if the student matriculates. The library, fellowships, loan funds, prizes, lecture foundations, student health service and many other facilities at the school are described in the November 1 issue of the *Bulletin* of the Western Reserve University School of Medicine.

Commencement Prizes at Washington University

At the 1941 commencement at Washington University School of Medicine, St. Louis, the following prizes were awarded: George F. Gill Prize in anatomy, $50, to Bryce Harold Bondurant; George F. Gill Prize in pediatrics, $50, to Jane Aral Erganian; Alpha Omega Alpha Book Prize to Leon Kahn; Howard A. McCordock Book Prize to Raymond Ray Lanier Jr.; Alexander Berg Prize in bacteriology, $100, to Herman Theodore Blumenthal and Hyman Bernard Stillerman.

The Alumni scholarship for the school year 1941-1942 has been awarded to Donald Huelsmann; the T. Griswold Comstock scholarship to Raymond F. Rose; the Andrew R. and Susie Fleming Fund award to Jean R. Boyle; the George F. Gill scholarships to Edward W. Czebrinski and Harold Grant; the Williams McKim Marriott Memorial scholarship to William J. Davis; the Eliza McMillan scholarship for women to Dorothy Reese; the LaVerne Noyes scholarship to Saul D. Silvermintz; the Robert Allen Roblee scholarships to

Robert E. Holt Jr. and Helen C. Reller; the Jewish Women's scholarships to Bernard Bressler and David Feldman, and the John B. Shapleigh scholarship to John H. Eisenhauer.

Two British medical students were admitted to the third year class as Rockefeller Foundation scholars. They are Ewan F. B. Cadman of Southport, Lancashire, England, and Matthew O'Hea of Wishaw, Scotland.

Northwestern

The annual Founder's Day Lecture at Northwestern University Medical School, Chicago, was given this year on October 7 in honor of Dr. Irving S. Cutter, the retiring dean. The new dean, Dr. James Roscoe Miller, gave the address which expressed for the school its appreciation of the work and life of Dr. Cutter, on whom at this occasion the president of Northwestern University conferred the degree of Doctor of Science. The faculty presented to Dr. Cutter a book containing the signatures of all its members and a message of gratitude.

A new course entitled "Military Medicine" has been added to the senior year; four lectures will be given by officers of the army and navy and twenty-eight lectures by specialists at Northwestern University on medicomilitary problems.

Student Clinic Day at Wayne

Regular classes were dismissed to permit students, faculty and alumni to participate in the fourth annual Student Clinic Day at Wayne University College of Medicine, Detroit, December 12. The students were in charge in the clinical sessions on heart sounds, high blood pressure, the electrocardiograph and contagious diseases. The general chairman was junior student Wellington B. Huntley. The program began at 8:30 a. m. and continued throughout the afternoon. Cash prizes and medals were awarded to the students who contributed outstanding papers or clinical leadership to the day's program. At the dinner meeting in the evening at the Wardell Hotel, S. L. A. Marshall of the Detroit *News* spoke on "The War Today." Other dinner speakers were Dean Edgar H. Norris, M.D., and Associate Dean William J. Stapleton, M.D.

A. O. A. at New York University

Under the auspices of the Delta chapter of Alpha Omega Alpha, Dr. William C. Stadie, associate professor of research medicine at the University of Pennsylvania School of Medicine, discussed fat embolism in diabetes mellitus on October 31. After the lecture the following newly elected members of the society were welcomed: Class of 1942: David A. Dreiling, Saul J. Farber, Arnold W. Friedman, Robert M. Gabrielson, Irma H. Gross, Carol K. Smith, Harvey P. Kopell, Harold Lief, Doris H. Milman, Alice E. Moore, David F. Sunkin; Class of 1943: Ernest Cotlove, Jerome Seides, Leon Sokoloff.

The Agramonte Manuscripts at Louisiana

Dr. Philip S. Hench, Rochester, Minn., who is preparing a monograph on the work of the U. S. Army Yellow Fever Commission, recently visited the Aristides Agramonte Memorial Library at the Louisiana State University School of Medicine, New Orleans, in order to examine manuscripts and papers of Dr. Agramonte, who was a member of the U. S. Army Commission that demonstrated the transmission of yellow fever by means of a certain species of mosquito. Dr. Hench had just returned from a visit to Dr. Agramonte's daughter in Havana, Cuba.

Syracuse

The new initiates into Alpha Omega Alpha at Syracuse University College of Medicine are William N. Hamblin, Paul Rousseau, Michael P. Rizzuto and Alson F. Pierce, all of the class of 1942, who together with J. Benton Pike and Erwin R. Centerwall, former initiates, comprise the active chapter at Syracuse. This organization will provide a series of programs open to the entire student body and faculty in which members of the local chapter will present scientific papers. At the first of the series for this year on November 13 J. Benton Pike gave a paper on renal hypertension.

Dr. Harry Goldblatt, professor of experimental pathology at Western Reserve University School of Medicine, Cleveland, discussed experimental hypertension, December 9, in the first of a series of lectures sponsored by the local chapter of Nu Sigma Nu medical fraternity and open to the entire student body.

The Harriman scholarship, which is awarded each year to one of the five top ranking students in the senior class, was awarded this year to Paul Rosseau.

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 2287:

1. Samuel Fuller (1580-1633), who studied medicine in Leyden. Dr. Fuller then practiced in New England until his death in 1633.

2. Dr. James Lloyd (1726-1810), who was born on Long Island, New York, and after a preliminary education in a private school at New Haven was apprenticed in medicine for five years to Dr. William Clark of Boston. He attended lectures on midwifery in London for two years and also acted as a "dresser" at Guy's Hospital in London, where he worked with William and John Hunter. He was in practice in Boston at the time the Revolutionary War broke out.

3. Thomas Thatcher (1620-1678), who also was installed as the first minister of the Old South Church in Boston, Feb. 16, 1670. He was educated for the ministry, according to Dr. Benjamin Spector's book "One Hour of Medical History," volume 5, by Charles Chauncy, the second president of Harvard College, and it is said he probably received his medical education from the same source. In 1677 he issued a publication entitled "A Brief Rule to Guide the Common People of New England how to order themselves and theirs in the Small-Pocks, or Measles."

4. David Livingstone (1813-1873), who studied medicine in London and in 1840 sailed on the first of his great expeditions to Africa. He was absent from England from that year until 1856, again from 1858 to 1864 and again from 1865 until his death at Ilala on Lake Bangweolo in 1873. He made many important geographical discoveries in Africa and was noted for his kindness and tact in dealing with the natives and for the intensity of his desire to open up Africa so that the slave trade might be brought to an end. Among his publications are "Missionary Travels and Researches in South Africa," in which is an accurate account of the tsetse fly disease, and "Narrative of an Expedition to the Zambesi and Its Tributaries, and of the Discovery of the Lakes Shirwa and Nyassa." The well known meeting in Central Africa of Dr. Livingstone with Henry M. Stanley, who had been sent by the New York *Herald* to find Livingstone, took place in October 1871. The house in which Livingstone was born has been purchased by public subscription to be preserved in honor of this great missionary and explorer.

Book Notices

Essentials of General Surgery. By Wallace P. Ritchie, M.D., Clinical Assistant Professor, Department of Surgery, University of Minnesota Medical School, Minneapolis. Cloth. Price, $8.50. Pp. 813, with 237 illustrations. St. Louis: C. V. Mosby Company, 1941.

The author admirably succeeded in condensing into a single volume the ever spreading field of general surgery. After a concise but comprehensive discussion of fundamental general problems such as anesthesia, surgical technic and asepsis, the common surgical lesions of different parts of the body, their diagnosis and methods of treatment are described in a masterly manner. No superfluous words are used, yet nothing is omitted that has a bearing on the subject. Although the book has been written primarily for the undergraduate student, it contains enough detail to have an appeal not only to a general practitioner but even to a surgeon who wishes to brush up on the latest advances in his selected field. Several chapters have been written by other members of the staff of the University of Minnesota Medical School, but all are characterized by the same features: brevity, clarity of presentation, easy style, good illustrations. Few errors and omissions of minor importance have been noticed. In the chapter on history of the development of surgery an inclusion of the names of Cushing, Chevalier Jackson and the Mayos would be advisable, because they widened the horizon of surgery in many directions. In the chapter on anesthesia, Luckhardt's name deserves a place because of the popularity of ethylene. "Hypertrophy is enucleated" (p. 724, fifth line from top) is incorrect phraseology, because hypertrophy is a pathologic process and not an organ which can be removed. Not only can the book be unhesitatingly recommended to undergraduate students, but undoubtedly it will make a fine acquisition to the libraries of general practitioners and surgeons as well.

Studies on the Etiology of Gallstones: A Subtilis-Like Bacilli-Group as an Etiologic Factor. By Karl Mårtensson. Akademisk avhandling för erhående av medicine doktorsgrad, Stockholm. Acta chirurgica Scandinavica, Vol. LXXXIV, Supplementum LXII. Paper. Pp. 227, with 74 illustrations. Stockholm: Nordisk Rotogravyr, 1941.

This is essentially a report of the results obtained in studies carried out to determine the relationship between bacterial infection and the formation of gallstones. The study was undertaken because it was noted that the center of gallstones was made up of necrotic-like epithelial cells and that, in the walls of gallbladders in which recent formation of stone had taken place, sporulating bacilli occurred intraepithelially and subepithelially with surrounding regions of necrosis and desquamating epithelium.

Considerable space is given to a general consideration of cholelithiasis. The composition and structure of gallstones is reviewed in detail, and a method is presented for analyzing the stroma of the gallstone without injuring possible existent bacteria. A chapter is devoted to the symptomatology and pathology of gallstones. The various theories of the etiology of gallstones are reviewed in detail, and attention is drawn to the possible connection between the formation of gallstones and systemic diseases and between the formation of stones and other disturbances. The literature is extensively reviewed in consideration of the various hypotheses advanced for the formation of gallstones.

Material for culture was obtained from diseased gallbladders removed at operation in 78 cases and at necropsy in 28 cases. A variety of organisms was isolated by this method, but the organism most often found proved to be a gram-positive, mobile endosporulating rod which the writer chooses to call the "typical bacillus." This "typical bacillus" was recovered from the wall of the gallbladder, the bile, the gallstone itself and the intestinal tract.

The organism discovered and called the "typical bacillus" was thoroughly studied as to morphologic and biologic characteristics, and it was found that it could be divided into three groups, two of which are facultatively anaerobic, one being an obligatory anaerobe. The organism did not fit any previously known bacterium in all its characteristics.

In vitro experiments showed that the "typical bacillus" was capable of causing precipitation of cholesterol when inoculated on sterile normal human bile. Definite gallstones were produced experimentally in rabbits, swine, sheep and cattle following the inoculation of cultures of this bacillus. All the types of biliary calculi found in man were obtained. "Typical bacilli" were cultured from gallstones experimentally produced, and these organisms when injected into animals were able to give rise to gallstones. The organism was administered directly into the lumen of the gallbladder, intravenously, subcutaneously or orally; all methods were effective in the production of gallstones.

An antigen was prepared with a spore free culture of dead bacilli, and rabbits were thus immunized against the "typical bacillus." In none of these rabbits did biliary calculi develop subsequent to the injection of gallstone producing doses of the bacillus directly into the lumen of the gallbladder. The author expresses the belief that this indicates that the formation of gallstones is affected by the specific antigen of the typical bacillus.

This report is interesting and deserves verification and further clarification by independent workers. The work seems to have been well performed and the results well controlled. The results obtained lend further evidence to substantiate the infectious theory of the formation of gallstones.

A Text-Book of Pathology. Edited by E. T. Bell, M.D., Professor of Pathology in the University of Minnesota, Minneapolis. Fourth edition. Cloth. Price, $9.50. Pp. 931, with 433 illustrations. Philadelphia: Lea & Febiger, 1941.

This edition follows the same general plan as the earlier editions. The first portion (approximately 40 per cent) is devoted to general pathology, the remainder to special pathology. The text has been increased by thirty-eight pages, and forty-one new illustrations have been introduced.

Certain commendable changes have been made. The chapter on diseases of the urinary system has been thoroughly revised, and Bell's classification of renal disease has been somewhat modified. The discussion of renal diseases remains probably the best to be found in any standard textbook. That portion of diseases of the heart which concerns congenital disorders has been rewritten and remains an excellent chapter. The chapter on diseases of the blood has been written by Bell in this edition but remains essentially the same as formerly presented by Hal Downey except for expansion of certain portions and a shift in emphasis from histogenesis to differentiation of blood cells.

The following criticisms seem worth recording: Although pathologic physiology has received considerable attention in this volume, such disorders as shock, hypovitaminosis, acid base unbalance and uremia receive but little attention. The problem of aging, which is receiving more and more general consideration, is not dealt with here. Bell's general discussion of tumors is excellent: his treatment of specific tumors, however, often includes insufficient histopathology. The general discussion of tuberculosis is probably inadequate for the beginning student. Hypertrophy, hyperplasia and metaplasia are not treated as fundamental processes. In Bell's discussion of edema it is unfortunate that certain outmoded physiologic concepts are retained and that more emphasis is not given to the role of injury in causing increased capillary permeability. Toxic cirrhosis has been inadequately treated, and cardiac cirrhosis is not mentioned. Only five lines are devoted to the general subject of focal necrosis of the liver; four times this much space is spent on cystic degeneration of the same organ. Another example of disproportionate emphasis is encountered in the two and one-fourth page discussion of malaria, in which but five lines deal with morphologic changes.

Worthy of special commendation are gynecologic pathology, diseases of the spleen and the mycoses. In these and other chapters a brief introductory review of histology and physiology is employed to good advantage. The subject of fundamental phenomena of inflammation is well presented by Bell, and his discussion of syphilis is very good. The illustrations are excellent from the point of view of both quality and selection. The bibliography which follows the discussion of each general subject has been well chosen and is particularly valuable because of the explanatory notes which accompany it. This will continue to be a valuable textbook of pathology, probably of greater usefulness to the advanced student, however, than to the beginner.

Über funktionelle Veränderungen der P- und T-Zacken im Elektrokardiogramm: Experimentelle Untersuchungen mit Ergotamin und Amylnitrit, sowie klinische Beobachtungen. Von Olof Nordenfelt. Acta medica Scandinavica. Supplementum CXIX. Paper. Pp. 186, with 17 illustrations. Lund: Håkan Ohlssons Boktryckeri, 1941.

In this extensive monograph with an English summary the author presents his investigations on the changes in the electrocardiogram due to certain functional disorders. He first reports on the effects of posture change from lying to standing in 49 subjects before and after the injection of 0.5 mg. of ergotamine. This included 14 patients with orthostatic hypotension. In all subjects, but more marked in the orthostatic patients, definite changes in the electrocardiogram appeared. Ergotamine was found to lessen noticeably the postural alterations in the electrocardiogram. This suggested that the action of posture change does not operate through the production of coronary insufficiency but through a direct action on the heart, reflex in origin and sympathicotonic in character. The author then relates his experience with the inhalation of amyl nitrite by 21 normal young persons and by an older person with complete heart block. Again changes in the electrocardiogram were found associated with the cardiac acceleration and drop in blood pressure, changes that resembled those seen in the orthostatic patients on posture change. On this account the author concludes that the mechanism in the two groups is the same.

In the next section he reviews the electrocardiographic changes following exercise carried out on 10 normal persons. The exercise consisted in running up to the point of marked cardiac palpitation. The electrocardiographic changes after exercise were similar to those in the preceding experiments and are again ascribed to an increase in the sympathicotonic state.

The author next reviews the literature on the influence of the autonomic nervous system on the electrocardiogram and then briefly discusses the physiology of coronary vessels. This analysis in the author's mind supports his previous contention of the neurogenic origin of the electrocardiographic changes. Since the vagi appear not to go to the ventricles, the changes seen following vagus stimulation is attributed to a decrease in the sympathicotonic state. Increase in the sympathicotonic state causes cardiac acceleration, a taller P wave especially in leads 2 and 3, a shorter PR, a slight depression of the S-T segment, a marked decrease in the size of the T wave which may become diphasic or inverted and a relative prolongation of electrical systole.

While the argument that coronary insufficiency is not involved in these electrocardiographic changes is supported by the author's experience, the possibility is not excluded in the opinion of the reviewer that the change in autonomic nervous tone may operate by changing the caliber of the coronary vessels rather than, as is suggested, by a direct action on the heart muscle. Nevertheless the view expressed by the author is one well worth considering.

Perhaps the most important contribution of this detailed study is the suggestion that 0.5 mg. of ergotamine given intravenously or subcutaneously may be used to differentiate between the reversible functional electrocardiographic changes and the irreversible ones based on organic disease of the heart. It is now clearly recognized that, in fear and in neurocirculatory disorders of the heart, electrocardiographic abnormalities are found resembling those seen in coronary insufficiency. A more extensive trial of ergotamine as suggested by the author may turn out to be of clinical value in the differential diagnosis. The experience of the author, however, is insufficient to warrant this final conclusion.

Microbes Which Help or Destroy Us. By Paul W. Allen, Ph.D., Professor of Bacteriology and Head of the Department, University of Tennessee, Knoxville, D. Frank Holtman, Ph.D., Associate Professor of Bacteriology, University of Tennessee, and Louise Allen McBee, M.S. Cloth. Price, $3.50. Pp. 540, with 115 illustrations, including 13 color plates. St. Louis: C. V. Mosby Company, 1941.

This book is another of the popular presentations of bacteriology as it relates to both the infectious diseases and the various phenomena of bacterial etiology that are beneficial to man. The material is soundly and clearly presented in an informal way and should be readily understood and enjoyed by the intelligent layman. The style is somewhat strained in the attempt to popularize, e. g. "our microscopic pals," but, though slightly irritating to the scientist, is perhaps desirable here. To one trained by systematic study of the bacteria, the organization of the book as a whole seems somewhat confused. For example, a number of chapters intervene between the discussion of water supplies and that of sewage disposal; bacteriophage is discussed in a separate chapter at the end of the book rather than with the viruses; the spirochetes of Weil's disease are widely separated from Treponema. Such an illogical development will, of course, be hardly apparent to the layman. Much of the material on the infectious diseases is discussed in terms of particular pathologic conditions. There are, for instance, chapters devoted to the bacteriology of appendicitis, conjunctivitis, boils and carbuncles, tooth infections and the like, all of heterogeneous etiology. Whether such an arrangement is to be preferred in a popular presentation to one of suppurative infections, infections of the upper respiratory tract, the enteric diseases and the like is open to question. In a few instances questionable statements are made; the genesis and development of the epidemic wave, for example, are accounted for entirely in terms of variations in virulence—a belief vigorously expounded by some but for which there is no direct evidence. Questionable statements are rare, however, and neither are serious nor do they detract from the presentation as far as the layman is concerned.

The book is well made and attractively bound. Portraits comprise a large part of the illustrations, and there are thirteen excellent color plates taken from other books issued by the same publisher. The black and white pictures are somewhat below standard, as a rule, but some, such as figures 9 and 10, are superb. The physician will find this book of little value as a source of information because of its elementary nature but may recommend it to the inquiring layman as a clear, accurate and informative discussion devoid of the attempts at sensationalism characteristic of some books of this kind.

Annual Review of Biochemistry. James Murray Luck, Editor. James H. C. Smith, Associate Editor. Volume X. Cloth. Price, $5. Pp. 692. Stanford University P. O.: Annual Reviews, Inc., 1941.

A book which has been almost indispensable since its inception in 1932 is the Annual Review of Biochemistry. This volume presents the status of certain subjects in the biochemical field in such terms that interest not only by chemists but by practically all laboratory and clinical investigators in almost every field of biologic science is the ultimate response. The present edition reviews the more recent developments in a number of biochemical subjects by offering twenty-four articles which have been written by authorities in their respective fields of endeavor. The topics are biologic oxidations and reductions, proteolytic enzymes, nonproteolytic enzymes, chemistry of the carbohydrates and glycosides, chemistry of amino acids and proteins, the chemistry and metabolism of the compounds of sulfur, carbohydrate metabolism, fat metabolism, the metabolism of proteins and amino acids, the biochemistry of the nucleic acids, purines and pyrimidines, the biochemistry of creatine and creatining, detoxication mechanisms, hormones, the water-soluble vitamins, fat-soluble vitamins, nutrition, relation of soil and plant deficiencies and of toxic constituents in soils to animal nutrition, mineral nutrition of plants, plant growth substances, spectrometric studies in relation to biology, review of bioluminescence, the chemistry and metabolism of bacteria, biochemical nitrogen fixation and properties of protein monolayers.

It is not possible in a book review to present more than a glimpse of the material contained in such an informative work as this volume. Those who are familiar with past editions will need no urging to peruse the pages of the present edition. Those who have not been very intimate with the companion volumes will be well repaid if they avail themselves of a copy. Members of the medical profession will be especially interested in the sections dealing with the metabolism of fat, proteins and amino acids, detoxication mechanisms, hormones, vitamins and nutrition. For example, in the section relating to hormones there may be found a survey of the present status of thyroxine, the adrenal cortex, progesterone, estrogens, androgens and the anterior pituitary gland. In general, each hormone is discussed under isolation and partial synthesis of derivatives, physiologic effects and assays. As in the past, this edition can be highly recommended as an authoritative treatise on recent developments in biochemistry, and a copy should be available for all lecturers, students and clinical and laboratory investigators.

The Man Who Lived for Tomorrow: A Biography of William Hallock Park, M.D. By Wade W. Oliver. Cloth. Price, $3.75. Pp. 507, with portrait. New York: E. P. Dutton & Co., Inc., 1941.

This is the biography of a man whose name has been associated with progressive preventive medicine and public health practices for almost fifty years. Dr. William Hallock Park began his career in this field as a member of the New York City Department of Health and there remained for forty-six years before retiring in 1936. As is so often the case with medical men who later become authorities in their respective specialties, Dr. Park had no intention of choosing this career when he graduated; on completing his internship he spent a year of special study in Europe, returning to begin the practice of otolaryngology. Because of a disagreement on the etiology of diphtheria voiced during a social call on Dr. Prudden, Park was invited to work in Prudden's quarters and there demonstrated that the Klebs-Loeffler bacillus is the cause of the disease. At that time this organism was not generally accepted as the responsible agent. This marked the beginning of a career that was to play an important part in public health.

Although many will remember Dr. Park as the first to produce diphtheria antitoxin outside of Europe, others will associate him with general measures on diphtheria control and with studies on cholera, tuberculosis, meningitis, encephalitis, poliomyelitis, pneumonia, whooping cough, streptococcic infections, rabies, tetanus, influenza, typhoid and other infectious hazards to public safety.

Author of recognized textbooks on bacteriology and hygiene and public health, Park's preeminence was cited on Oct. 6, 1936, when the William Hallock Park Laboratory of the New York City Board of Health was dedicated in honor of his retirement as director of laboratories. Among the letters forwarded to Park on this occasion was one from the late Dr. Hans Zinsser, who wrote "Your accomplishments in the introduction of diphtheria antitoxin in this country and in the organization of what was then the model public health and research laboratory in the United States are matters of record, but there are other things you have done which are known only to those of us who were influenced by your example, your advice and your personality. There are many of us—but few who owe you more than I do." Holder of numerous awards and honors, one of which was knighthood bestowed by King Alfonso XIII of Spain, he enjoyed an international reputation that is well described in this biography.

The author is to be congratulated on his practice of frequently quoting from correspondence concerning events which transpired in Park's life. This serves the twofold purpose of emphasizing the work of a leader in public health and of affording interesting and authentic reading in a fashion not commonly found in current biographies. It is a book which is a worthwhile addition to any library, as it presents more than the story of one man's life; it offers interesting sidelights on the development of many of the preventive medicine measures now employed in the United States and elsewhere.

Torch & Crucible: The Life and Death of Antoine Lavoisier. By Sidney J. French. Cloth. Price, $3.50. Pp. 285. Princeton: Princeton University Press; London: Oxford University Press, 1941.

Lavoisier is best known as "the father of modern chemistry," but he was one of the leading men in his day for other reasons as well. He was formally educated for the law but had more interest in science, especially geology, water supplies and water, with the result that he was elected member of the Academy of Science at the age of 25. In his work with water and gypsum he weighed his materials with the greatest care, a new quantitative procedure that in his hands led to the overthrow of the centuries old phlogiston dogma of combustion and to the introduction of quantitative methods in chemistry, by means of which he discovered the composition of the air and its relation to life. His investigations laid the foundations of chemical physiology. He changed completely chemical thought and nomenclature. We owe the names oxygen and hydrogen to him. But in addition to his epochal achievements in the science of chemistry Lavoisier, always an active citizen with liberal and progressive tendencies, gave much time and energy to work of a public nature. He held membership in the "Tax Farm" (Ferme générale) of France and was a member of its committee on tobacco. When the government took over the powder monopoly Lavoisier became the director of the powder commission and moved his residence and laboratory into the old arsenal of Paris. Here Madame Lavoisier presided with grace and charm over famous dinners. And Lavoisier had a country estate where he made successful experiments in agriculture and endeared himself to the people of the district. In his biography French has succeeded admirably in his attempt "to write in one person the elements which made Lavoisier such a striking figure." He gives us a vivid, absorbingly interesting account of the rise of Lavoisier's family, his personal life, character and career, in science as well as in public service and other relations. A strong light is thrown on the tremendous developments in the background that led to his execution, May 8, 1794, a victim of the revolutionary fury. He was then 50 years old. "It took but an instant to cut off his head; a hundred years will not suffice to produce one like it."

Professional Adjustments. I. By Gene Harrison, A.B., R.N., Educational Director, Druid City Hospital School of Nursing, Tuscaloosa, Alabama. Cloth. Price, $2.25. Pp. 204. St. Louis: C. V. Mosby Company, 1941.

A student nurse, or better still a prospective nurse, will find this book of the utmost value to her. Based on the extensive experience of the author as a teacher of nurses and director of nursing schools, it deals with the everyday, commonplace matters which, taken separately, are of little consequence but which, added together, may make all the difference between a good nurse and an inferior one. Dealing with such matters as careless habits of speech, neatness and general conduct and discussing rouge, fingernail polish and other matters pertaining to appearance, it relates all these to the fundamental question as to what effect they will have on the character of the nurse and her service to the patients. In the same way the matter of alcohol, tobacco, chastity, personal relationships with fellow students and fundamental honesty of attitude toward hospital, patients, doctors and self are treated in a straightforward, simple, sincere manner which should be of genuine help to any student nurse. This book not only should be read by student nurses but might profitably be reread by some graduates and should certainly be recommended to the girl who looks on nursing as a prospective career. Since the book is intended for use in a course of instruction, it is organized into chapters to each of which is appended a list of suggestions for study and a bibliography for reference reading, as well as one or more pages for personal notes. An inspirational touch is furnished by a brief quotation opposite the opening page of each chapter. There is a good index.

The Baker Memorial: A Study of the First Ten Years of a Unit for People of Moderate Means at the Massachusetts General Hospital. By Haven Emerson, M.D. Cloth. Price, 50 cents. Pp. 75, with 2 illustrations. New York: Commonwealth Fund, 1941.

In 1930 the Baker Memorial Hospital introduced a plan for the hospitalization of middle class patients. The patient day rates were to be between $4.50 and $6.50 and the medical bill limited to approximately $150 for any patient. In the ten years that followed, bed capacity has increased from one hundred and fifty-nine to two hundred and forty-nine and the percentage of occupancy from 54 to 86. The death rate has been about midway between that of the Massachusetts General Hospital and the Phillips House, with which institutions it is affiliated. Massachusetts General cares for charity patients and the Phillips House devotes itself to private patients. A questionnaire to discharged patients brought general expressions of satisfaction as to the treatment received with criticisms mainly confined to administrative details. The average patient payment during the ten year period for all inclusive hospital care was $119.09 and the average medical fee $66.06. While the Baker Memorial Hospital shows a small operating surplus, account has not been taken of depreciation or of sums contributed from the resources of the Massachusetts General Hospital. A considerable sum has also been contributed by the Julius Rosenwald Fund. There is no retirement or insurance plan for the administrative or nonprofessional staff. In view of the gift of $2,000,000 for the original building and numerous other large gifts to meet deficits, it cannot be said that the Baker Memorial Hospital plan offers a pattern which can be followed generally.

Organic Chemistry with Applications to Pharmacy and Medicine. By Eldin V. Lynn, Ph.D., Professor of Chemistry, Massachusetts College of Pharmacy, Boston. Cloth. Price, $4.50. Pp. 410. Philadelphia: Lea & Febiger, 1941.

For some years there has been need for a textbook on organic chemistry especially prepared for students who are engaged in the study of organic chemistry as an adjunct to pharmacy and medicine. This volume has been written to fill this need. The subject matter includes that usually found in organic treatises, but most of the material which is only of commercial or theoretical interest is omitted, while that which is of pharmaceutic or medical interest is emphasized. U. S. P., N. F. and N. N. R. products are so designated and their descriptions given, but only cursory reference is given to methods of analytic procedure.

The subject material is well arranged and a sufficient number of formulas and illustrations are given for clarification of the reactions. The organic compounds are divided into forty-four chapters according to chemical structure; the general characteristics of each group are given and important members are described individually. At the end of each chapter there are a number of review questions which deal mainly with reactions and identifications. In the interest of brevity, the descriptions not infrequently assume the character of an outline, which results in a lack of smoothness of presentation.

The book is of especial value to those organic chemistry teachers who have not had training in the medical or pharmaceutic fields and find difficulty in giving supplementary lectures on these subjects. To the student of medicine or pharmacy it is a textbook the contents of which can be studied as a whole without the necessity of omitting portions that are too far afield. Therefore it will be found useful not only as a book for the classroom but also as a reference work.

Health Resorts of the USSR: A Symposium of Articles Compiled from Data of the Central Institute of Balneology in Moscow. Editor: Dr. I. A. Pertsov. Cloth. Pp. 271, with illustrations. Moscow: The U. S. S. R. Society for Cultural Relations with Foreign Countries (V. O. K. S.), [n. d.]

This book leaves the reader in some doubt as to whether it is intended to promote the health resorts of the Union of Soviet Socialist Republics or to extol the October Socialist Revolution. It consists mainly of descriptions of various health resorts in the different autonomous Soviet Republics. These descriptions are almost purely promotional; one searches in vain for true scientific evaluation. For example, with respect to the resort Akhtala, one of the Georgian Soviet Socialist Republic's resorts, occur the following quotations, which are typical of the book:

> Exuding from the hills, with a temperature of about 23°, the Akhtala muds have been found to consist of water and solid substances among which plastic clay predominates. The aqueous component of the mud is basically sodium chloride water, also containing carbonates of sodium, calcium, magnesium and so on, its mineralization totaling 16.5 Gm. per liter.
>
> Akhtala mud is administered both in the form of hot baths and by bathing at the mud-mounds. It finds application for the treatment of diseases of the locomotor organs, chronic perigastritis, periduodenitis, hepatitis, perityphlitis, neuritis and neuralgia. These muds are also a remedial for treatment of skin diseases, chronic phlebitis, varicose ulcers, female diseases and other ailments.

Much space is devoted to pointing out the tremendous growth and reconstruction of the "culture and rest" facilities which are claimed to be open to all Soviet workers. The actual capacities and figures given for occupancy during recent years indicate that even yet these facilities are actually open to only a small percentage of those who are theoretically entitled to them.

This book is nothing more than a descriptive listing of Soviet spas with propaganda material for the Soviet political and economic system.

Immunity Against Animal Parasites. By James T. Culbertson, Assistant Professor of Bacteriology, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $3.50. Pp. 274, with 4 illustrations. New York: Columbia University Press, 1941.

The author intends this volume to be of value to those beginning the study of the fundamental principles of immunity in relation to the parasitic forms of life, but he assumes that the reader is well versed in the fundamentals of both parasitology and immunology.

The contents of the book are divided into an introduction and three parts: part one relates to resistance and acquired immunity, part two relates to immunity in specific diseases and part three discusses applied immunology. In addition there is included a list of the abbreviations of names of periodicals and an adequate index. Part one discusses natural resistance, age resistance, specifically acquired immunity, requisites for immune response, parasites which elicit immunity, mechanisms of specific immunity and demonstrations of immunity; part two describes the immunity from the amebiases, the leishmaniases, the trypanosomiases, the malarias, the coccidioses, the trematodiases, the cestodiases, the nematodiases and the arthropods and part three contains a classification of parasites, a description of vaccination against parasites and diagnosis of parasitic infection. The index is sufficiently extensive to permit easy reference.

The style of writing and the general makeup of the book are conducive to pleasant reading. Unnecessary details are kept at a minimum. The information contained in this book will be of interest and value to all students of immunity against animal parasites, and the volume can be regarded as an authoritative source for reference. Its availability in all libraries will be appreciated by students and lecturers.

A Laboratory Manual of Physiological Chemistry. By D. Wright Wilson, Benjamin Rush Professor of Physiological Chemistry, University of Pennsylvania, Philadelphia. Fourth edition. Cloth. Price, $2.50. Pp. 298. Baltimore: Williams & Wilkins Company, 1941.

The book is designed as a laboratory manual for medical, dental and other students taking a general course in biochemistry. It follows essentially the same pattern as the three previous editions, which were reviewed in THE JOURNAL. Obviously the manual has been written primarily to meet the author's own requirements in teaching relatively large classes in biochemistry. Since the general plan remains unchanged, he has undoubtedly found that the book meets these requirements. The right hand page has been left blank for laboratory notes, thus cutting in half the number of apparently printed pages. The manual is confined almost wholly to directions for laboratory experiments, discussion and explanations being reduced to a minimum with the obvious intention of focusing the students' attention on the laboratory experiments. The directions are concise but given in sufficient detail so that they can be followed and understood. In general the course appears to follow the plan introduced by the Chittenden-Mendel school. The methods selected may be called standard methods. The author has been conservative in that the many advances in the field have resulted in few changes in the manual. He has apparently felt that, if the laboratory work furnished the student a sound ground work in the subject, other necessary material could be given in lectures and assigned readings. It is of interest and logical that he should have included carbohydrates, proteins and fats in part I, introduction, along with inorganic constituents, standard acid and alkali, electrolytic dissociation, colloids and alcohols, aldehydes and esters. Part II, which takes up the last two thirds of the book, includes the usual topics covered in biochemistry under the heading of Body Tissues and Fluids. A short discussion of photoelectric colorimetry has been included in this edition.

Basic Problems of Behavior. By Mandel Sherman, M.D., Ph.D. Cloth. Price, $3. Pp. 440. New York, Toronto & London: Longmans, Green & Co., 1941.

This is a textbook for educators, psychologists and students of the social sciences. It is an elaboration of the author's Mental Hygiene and Education, published in 1934. The book aims "to present the clinical, experimental, psychological and psychiatric data of a number of basic problems of behavior." Individual chapters on the emotions, motivation and frustration, theories of personality, common mechanisms of adjustment, measurement of personality, attitudes and conflicts are followed by more clinical chapters on delinquent behavior, the neuroses and "mental abnormalities." The scope of the book is so broad that detailed critical review is here impossible. The author draws on his research and clinical experience and he culls and interprets the extensive literature, publishing a useful and well selected bibliography. The thesis that clinical and experimental observations or evidence can well be combined in the study of behavior is defended, but at times the author's prejudices lead him to turn against this point of view. This is particularly noteworthy in his repudiation of some psychoanalytic concepts which are "accepted on clinical evidence and . . . on com-

mon sense grounds" without "experimental or verifiable evidence" (p. 129). The implication is that psychoanalytic clinical observation is not verifiable. It is understandable, in view of the extensive range the book covers, that at times the discussion seems incomplete or superficial. The book is more authentic in the earlier chapters than in the later discussions of neuroses and psychoses. As an instance the author understates by far, if he at all appreciates, the role of aggression in the neuroses. The discussion of the neuroses is general and somewhat confused. The book will be useful to the general student of behavior as offering an orientation and guidance, particularly with respect to the literature. The medical student or student of psychiatry will find it of more limited usefulness.

Breathing Capacity and Grip Strength of Preschool Children. By Eleanor Metheny. George D. Stoddard, Ph.D., Editor, University of Iowa Studies, Studies in Child Welfare, Volume XVIII, No. 2. Paper. Price, $1.35. Pp. 207, with 7 illustrations. Iowa City: University of Iowa Press, 1940.

Grip strength, as measured with a hand dynamometer, and "vital" capacity, as measured with a spirometer, are two of the oldest and most popular tests for what is vaguely described as physical fitness. Precisely what is measured in each case and what may be the significance of the measurements are questions still unanswered by the present monograph. It is, however, of value to examine the results of such measurements. Dr. Metheny's book is a critical review of previous work and an exhaustive presentation of findings in 206 children between the ages of 2½ and 6½. Correlations were computed for the relation of grip strength and vital capacity with various anthropometric measurements as well as with "health ratings," "fatigue ratings" and school absences. Values for normals, repeatability and change with growth are presented. Some slight relation between grip strength and "health" was noted, but vital capacity showed no such relation. There was also an indication that a decline in grip strength may precede the appearance of active infection of the upper respiratory tract. The present monograph is a record, in extenso, of meticulous observation and statistical computation. It is not likely to provide stimulating or even very informative reading to the average physician or scientist but should be invaluable to those few investigators who are seriously concerned about the details of simple grip strength and vital capacity tests. We may hope that factors such as the start of infection, which may produce sudden changes in grip strength, will be studied further and presented in more reasonable compass.

Medical Policies and Procedures for the Resident Staff of the Alameda County Hospitals and Clinics. Benjamin Warren Black, M.D., Medical Director of Alameda County. New edition. Cloth. Pp. 123. Oakland, California, 1941.

This manual is well abreast of modern practice, having been revised annually since its first publication in 1936. It is conveniently arranged in loose-leaf form with eighteen chapters covering general hospital information and instruction to the resident staff as regards the admission of patients, laboratory and x-ray service, clinical photography, anesthesia, accidents and emergencies, and the general management of individual clinical departments, including isolation and psychiatry. Suitable reference is made to the use of the sulfonamide drugs, the administration of parenteral fluids, transfusions, vitamin therapy and other special procedures, and a section of twelve pages devoted to the symptoms and treatment of poisoning gives information that is exceedingly valuable to the intern and resident staff. There is likewise a convenient index of medical procedures and a list of the drugs and preparations available in the hospital pharmacy. This handbook of medical and administrative procedures prepared by a physician prominent in the field of hospital administration might well be used as a model for other institutions planning to establish new rules or modify existing regulations appertaining to the house staff.

The Rockefeller Foundation, International Health Division, Annual Report 1940. Paper. Pp. 247, with illustrations. New York, [n. d.].

Each year the International Health Division of the Rockefeller Foundation publishes an annual report with information on the technical side of its work and with references to descriptions of its research work presented in the medical literature. The report is purported to be prepared for the health officer, the public health student and readers interested in preventive medicine. Of the one hundred and fifty-two references analyzed and reported in the present edition, fifty-two relate to malaria and thirty-two to influenza. The contents of this annual report include an introductory statement covering the general activities of the division, a section on virus studies, a description of work on the control and investigation of specific diseases which include yellow fever, influenza, tuberculosis, syphilis, rabies, malaria, schistosomiasis, hookworm anemia, the common cold, scarlet fever, typhus fever, mental hygiene and nutrition, a summary of aid given to state and local health services, a description of the division's support to public health education, and a detailed account of expenditures. A table of contents together with an exceptionally adequate index provide a source of ready reference to the contents of this report. For a rapid perusal of the activities and studies undertaken by the staff of the International Health Division of the Rockefeller Foundation, this report offers a concise and clear source of reading. While the booklet will mainly appeal to those who are engaged in public health work, it contains many references of such international interest that no one will regret the time spent in passing over the pages.

When to See Your Doctor. By Robert S. Srigley, M.D. Paper. Price, 35 cents. Pp. 44, with illustrations. Columbus: College Book Company, 1941.

This pamphlet contains eight chapters dealing respectively with pneumonia, cancer, appendicitis, intestinal obstruction, diabetes, pulmonary tuberculosis, syphilis and heart disease. These chapters have been reviewed prior to publication by eminent physicians. Nevertheless the reviewer considers the treatment sketchy and inadequate. The title of the booklet, "When to See Your Doctor," taken in conjunction with the table of contents listing eight diseases, implies that only in these diseases does the author recommend seeing the doctor. The approach tends to favor self diagnosis, whereas the patient should be made conscious only of his own experiences which he can readily observe, even though he cannot interpret them. It is difficult to see how this booklet can contribute anything to the average patient's ability to decide when he ought to see his doctor and when he can safely procrastinate in the hope of spontaneous recovery.

A Text-Book of Bacteriology. By R. W. Fairbrother, D.Sc., M.D., M.R.C.P., Director of the Clinical Laboratory, Manchester Royal Infirmary, Manchester. Third edition. Cloth. Price, $5. Pp. 451, with 6 illustrations. St. Louis: C. V. Mosby Company, 1941.

An introduction to this book has been written by F. E. Colien of Creighton University School of Medicine. The book is divided into three parts. Part 1 concerns general bacteriology and consists of twelve chapters; part 2 deals with systematic bacteriology and considers the specific infectious agents, which are discussed in twenty-two chapters; part 3 concerns general technic, which is considered in three chapters. The author has omitted the word "medical" from the title of this edition, since the book has been used by junior students of bacteriology in faculties other than those of medicine although the author primarily intended it for the medical student. There is no bibliography given, which makes the book useless as a reference guide. The illustrations are good and the tables are concise and very useful to the student in differentiating infectious agents. The book should prove useful to the medical student.

Roentgen Technique. By Clyde McNeill, M.D. Second edition. Cloth. Price, $5. Pp. 329, with 276 illustrations. Springfield, Illinois & Baltimore: Charles C. Thomas, 1941.

The second edition of this treatise on roentgen anatomy and positioning is clearly designed for the physician, not for the x-ray technician. There has been added even more diagnostic material, and descriptions of technical procedures, which should be performed only by a physician, are a prominent feature. In an admirably concise style the author describes such relatively new x-ray methods as fluorography, body section roentgenography and cholangiography. The present edition also contains a section on fluoroscopy with particular attention to the dangers of this procedure. The methods of fluoroscopic localization of foreign bodies are well described. Pineal localization, pelvic and cephalic measurements, roentgen kymography and bronchography are treated in some detail. The additions and changes have increased the utility of the book. Its greatest value lies in the accurate manner in which x-ray positioning of all anatomic parts is described and illustrated.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

VITAMINS AND COLDS

To the Editor:—**Could you give me some advice regarding the advisability of giving vitamin preparations to industrial workers for the prevention of colds? Has there been any authoritative work done which indicates that any of the vitamins given to large numbers of workers will materially reduce the incidence of infections of the respiratory tract?**

M.B., Toronto, Canada.

ANSWER.—Some work has been done on the relation of vitamin A to colds and to other infections of the respiratory tract. None of the other vitamins have been extensively tried, doubtless because there is no reason to suspect that they might be of any value. The evidence so far available shows clearly that administration of vitamin A or vitamins A and D combined has no beneficial effect in reducing the incidence of colds. There is some evidence, but it is not at all conclusive, that the administration of vitamin A, while it does not protect against colds, does seem to lessen the severity of the attacks. The evidence is not conclusive enough to justify any claim that administration of vitamin A would be of benefit in preventing colds or other infections of the respiratory tract.

ABSORPTION AND EXCRETION OF MERCURY

To the Editor:—**A man was treated for syphilis over a period of several months with mercury inunction and some mercuric cyanide intravenously. He later suffered first and second degree burns over parts of his upper torso, and he died about twenty hours later. Postmortem examination showed 8 to 10 grains (about 0.6 Gm.) of metallic mercury in his liver and kidneys. He had had no mercury for several months prior to death. I wish to get all the available information as to the length of time mercury will remain in the tissues of the body after treatment is suspended.**

H. S. J. Walker, M.D., Mobile, Ala.

ANSWER.—It is unfortunate that more complete data are not furnished as to the amount and dosage of the mercury inunctions and of the injections.

After intravenous mercurial injections the metal not excreted will consist of two parts: (*a*) the portion still circulating in the blood stream and (*b*) mercury that is stored. The circulating mercury reaches its peak level within a matter of hours or certainly days after an intravenous injection of the cyanide or of the oxycyanate, so that several months later any residuum would be found only as stored metal in various organs, principally in the kidneys and liver.

With mercurial inunctions, much of the ointment that is rubbed on is never absorbed, as it is only the portion that is rubbed into the hair follicles that is absorbed and of course this only slowly. It is for this reason that the recommendation has always been made with inunctions that the patient should keep rubbing for thirty minutes by the clock. Even then much of the ointment will be left on the skin, and the physician is never sure just how much has been absorbed. Moreover, the absorption after mercury inunctions is much slower than after intravenous injections of a soluble mercury salt.

Cole, Sollmann and Schreiber compared the urinary mercurial excretion after daily intramuscular injections of mercury sodium bromide (5.5 mg. of metallic mercury) with 4 Gm. daily inunctions of strong mercurial ointment (50 per cent of metallic mercury). At the end of the first week excretion of mercury in the inunction patients was one-half that in the patients on injections. At the end of the second week the level of excretion was about the same. At the end of four weeks excretion in the inunction patients was twice as much. This indicates the slow absorption of the fine globules of mercury from the hair follicles. So that excretion in an inunction case continues at a high level for at least a week after therapy is stopped and in 1 case there was a daily excretion of 0.3 mg. fifty days after all inunctions had been stopped.

However, these are small amounts, and it is understood that the patient in question had had no treatment for several months prior to death.

It certainly would not be possible for a man to live and go about his daily duties for several months with 8 to 10 grains of metallic mercury in his body. Lomholt (Quecksilber, Theoretisches, Chemisches und Experimentelles, *Handb. d. Haut- und Geschlechtskr.* **18**:1, 1928) thinks that the saturation of mercury that may be reached in the body without harm would be around 100 mg. (less than 2 grains). It would seem that some other source must be looked for to explain such a large amount of mercury as was found in this patient.

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SULFANILAMIDE DERIVATIVES AND URINARY CRYSTALS

To the Editor:—**Is there any drug which may be given a patient with bronchiectasis who is taking sulfathiazole that will prevent the appearance of crystals in the urine?**

Edward K. Disney, M.D., Tucson, Ariz.

ANSWER.—The appearance of crystals in the urine of a patient who is receiving sulfapyridine, sulfathiazole or sulfadiazine is not of special significance unless the crystals are accompanied by microscopic or macroscopic hematuria. It is to be remembered that in patients receiving moderate to large doses of one of these drugs the urine is liable to be saturated or even supersaturated with the drug, and hence crystals may be seen in freshly voided specimens of urine. If such saturated specimens of urine are placed in the cold, as almost always takes place in hospitals where the early morning urine specimen is placed in an ice box and allowed to remain there for several hours before being examined, crystals of the acetylated or free form of the drug can almost always be found and of course are of little significance. Recently, Schwartz and his co-workers (THE JOURNAL, Aug. 16, 1941, p. 514) have reported that the administration of sodium bicarbonate in amounts equal to that of the drug (sulfathiazole) being prescribed reduced the number of instances in which crystals appeared in the urine and also, apparently, the number of crystals of this drug in the urine. While it is not a good practice routinely to administer sodium bicarbonate with sulfapyridine, sulfathiazole or sulfadiazine, it would appear from the work of Schwartz and his associates that under certain conditions the maintenance of high alkalinity of the urine will decrease the amount of crystals in it.

PROBLEMS IN TREATMENT OF SYPHILIS IN FAMILY

To the Editor:—**A man aged 32 has been found to have neurosyphilis, probably a brain gumma, with a history of primary infection seven years ago; he took a few treatments and then got married. He has a child 6 years old, another 3 years and another 8 months. A Wassermann test on the mother shortly before the 8 months baby was born was 4 plus (taken elsewhere); she received a few treatments before the child was born. Wassermann tests on the mother now are negative; so are they on the 8 months child and the 3 year old child. The 6 year old child is 4 plus. How can one account for this and what procedure should I take? Of course the mother should have a spinal fluid Wassermann test, but should the two negative children? Should these three be treated anyway or should one wait a while and take more Wassermann tests? If to treat them, how should it be done? Should one start the 6 year old girl on neoarsphenamine, sulfarsphenamine or bismuth and mercury preparations? The father is on iodides and a bismuth preparation now. After a course of this, it was felt that he should have fever therapy, probably by malarial inoculation. Would this be the proper procedure to follow in his case? This man also gave a transfusion one year ago to a 10 year old girl suffering with acute osteomyelitis. A Wassermann test taken by this girl now is 4 plus. Her osteomyelitis has never satisfactorily cleared up, and could this not be the reason? Also what treatment should one start her on?**

M.D., Iowa.

ANSWER.—In regard to the mother: The fact that her serologic reaction is positive and her oldest child also has positive serologic tests indicates, of course, that she has syphilis. The other two children apparently do not have syphilis, if there is no clinical evidence of the disease in them and their serologic tests are negative. Not every child born of a syphilitic mother necessarily has syphilis; in fact, about one half of the children born to syphilitic women will not have the disease. This can best be explained by the fact that Spirochaeta pallida did not pass through the placenta to the fetus, probably because the mother had developed a latent phase of syphilis and had few, if any, spirochetes in her blood stream. It does not seem necessary to make a spinal fluid examination of the two negative children, but it would be advisable to repeat the serologic tests of the blood at six month intervals for several years. The mother and the oldest child should have spinal fluid examinations.

The two younger children do not need treatment unless they should manifest in the future signs of or a positive serologic test for syphilis. The mother and child should be treated by

the so-called continuous system with mapharsen and a bismuth compound, the mother to receive increasing doses of mapharsen from 0.01 to 0.04 Gm. at five to seven day intervals for eight injections, while the child is given the same drug with dosage of from 0.005 to 0.02 Gm. The bismuth course should follow the mapharsen, 1 cc. being given four days to the mother and 0.5 cc. to the child for a series of sixteen injections of bismuth; at the completion of this, the second course of mapharsen may be started. This program is continued until four courses of mapharsen and six courses of bismuth have been given.

The treatment of the father is dependent on the response he manifests clinically as well as in the spinal fluid to chemotherapy. If after a fair trial, that is, two courses of an arsphenamine and bismuth, improvement is not obvious, fever therapy should receive serious consideration.

The osteomyelitis may or may not be of syphilitic origin, and the child's infection may be either congenital or acquired. A decision in this regard is impossible on the data presented and might require further examination. Not infrequently a syphilitic osteomyelitis will fail to heal under antisyphilitic treatment because the bony sequestrum remains and acts as a foreign body. An x-ray examination following antisyphilitic treatment should determine whether a sequestrum is present and whether its surgical removal is indicated. If the child has not been treated she may be placed on a program as just outlined for the child with syphilis.

NONTROPICAL SPRUE

To the Editor:—**What is the treatment at the present time for nontropical sprue and how does the disease vary from the tropical form? I have been using reticulogen and a fat free diet, but I cannot seem to stop the gradual weight loss which is occurring. Are any of the bile salts of use in the disease?**

M.D., New York.

ANSWER.—Tropical or endemic sprue is a chronic afebrile diarrhea occurring in rather limited tropical or subtropical areas and characterized by interference with intestinal absorption resulting in chronic starvation and wasting. The basic pathologic condition is one of nutritional deficiency gradually producing functional and then organic changes. The original deficiency is conditioned by other interwoven deficiencies, by infection and by various physiologic factors, such as in the endocrine system. The peculiar endemic distribution is unexplained. The classic symptomatic and clinical pathologic features rest primarily on a state of chronic starvation.

Nontropical sprue differs in having a nonendemic distribution, usually a more serious course and prognosis, a greater tendency to hemorrhage and much greater resistance to treatment methods which are highly effective in true or endemic sprue. Many consider the two conditions identical. Many others believe they are closely related, perhaps overlapping in etiology, but sufficiently distinct to constitute two different syndromes. Neither has an exact and invariable clinical picture, and in neither are exact pathognomonic criteria of diagnosis available.

Endless discussion goes on as to the relation of sprue to nontropical sprue, celiac disease, chronic pancreatitis, combined system disease of the cord, pellagra and pernicious (Addison-Biermer) anemia.

The principles of treatment in nontropical sprue are the same as for endemic sprue. They may be outlined as follows:

1. Diet should omit all sugar and reduce starch to a minimum. It should be primarily high in protein. N. H. Fairley's formula starts with a food ratio of protein 1, fat 0.3 and carbohydrate 1.3. With improvement this is gradually increased to protein 1, fat 0.36 and carbohydrate 2.0. Free use should be made of ripe bananas, banana flour, strawberries, whole fresh milk or goat's milk, beef juice and rare beef and such fruits as papaya if available.

2. Unconcentrated (old) liver extract should be given intramuscularly 5 to 10 cc. daily for twenty to forty days.

3. When hydrochloric acid is decreased in the gastric juice, diluted (U. S. P.) hydrochloric acid should be given, 4 cc. in a glass of whole milk with each meal.

4. Vitamins B_1, B_2 and D should be given in large quantities by mouth. If ascorbic acid is below normal in the blood, it should be given, 25 to 50 mg., in the vein.

5. Calcium should be supplied as dicalcium phosphate or basic calcium triple phosphate, 12 Gm. daily by mouth. Kaolin and bismuth subcarbonate may be added for severe diarrhea.

6. For flatulence, hot stupes, very hot baths and repeated small doses of castor oil (2-4 cc.) can be used.

7. Mild sedatives are often needed. Iron preparations, such as iron and ammonium citrates 0.5 Gm. thrice daily, are often needed to complete cure of the anemia. Repeated blood transfusions are often most beneficial. Bile salts are used in moderate dosage in the hope of improving intestinal absorption.

CHRONIC MYELOGENOUS LEUKEMIA AND PREGNANCY

To the Editor:—**A primapara aged 38, married sixteen years, has a normal menstrual history of five day duration with but little pain. There have been no miscarriages. She is a heavy set type about 5 feet 5 inches (165 cm.) tall and has a normal weight of 138 pounds (62.6 Kg.). Her past history is essentially negative. In April 1939, she had an ulcer on the anterior aspect of the left tibia. After several office treatments without improvement a biopsy was made and the pathologist reported a cutaneous cancer. This cancer was removed by the paste method, the wound apparently has healed, and there do not seem to be any bad effects. In June 1941, fifteen months later, the patient noticed that her feet were swelling and that she had considerable abdominal distress. She also complained of being tired and described her condition as a sort of indigestion, which lasted for several months. In September, about four months later, a swelling occurred at the point of the navel. After her physician observed this for several days, he diagnosed an abscess, which he opened in the office. Immediately a severe hemorrhage occurred. As it was impossible to control the bleeding at the office, the patient was taken to the hospital and given an anesthetic. Many sutures were put in the abdominal wall around the incision to get the bleeding stopped. The perplexing question as to why the patient should bleed so profusely arose at once, and, after a careful examination and blood checking, it was found that she was suffering from splenomyelogenous leukemia. Immediately roentgen treatments were administered to the spleen, and various blood counts were taken from time to time. The treatments have considerably reduced the white blood cell count. The patient has been taking a liver-stomach concentrate with iron and vitamin B complex by mouth, as well as liver hypodermics, and a general improvement has been noticed in her condition. She feels well and does all of her home work. About a year later, April 15, 1941, was the last day of her normal menstrual pereiod, and she received several roentgen treatments of the spleen at this time. In May and June, when she did not menstruate, she was advised by the doctor who gave her the roentgen treatments that it was probably the treatments that had caused the cessation of the menses. After missing two periods she came to my office, June 15, 1941, weighing 141 pounds (64 Kg.), the blood pressure 125 systolic and 70 diastolic, the Kolmer and Kahn reactions negative, the urine normal and much pleased with her general well being. I found her pregnant. She asked me if a pregnancy would have any bearing on a splenomyelogenous leukemia. In August the blood pressure and urine were normal and she had a 4 pound (1.8 Kg.) increase in weight but was still feeling fine. When she plays golf she exerts somewhat she has a pinkish vaginal discharge, and, of course, she was advised to give up golf and be more careful. On August 14 (four and one-half months after her normal menstrual period) she felt motion for the first time. The question of treatment of the patient and the prognosis are perplexing. Should the patient be given a chance at normal labor provided she has a normal course to the time of expectancy or should she have a cesarean section performed a short time before expectancy? Will continued roentgen treatment, which seems to be necessary to keep the white blood cell count down, cause unfavorable reaction to the fetus, and will it have any effect on the well being of the fetus? Would the administration of snake venom, vitamin K, congo red or the like be of any benefit to the patient before labor?**

G. C. Bates, M.D., Independence, Kan.

ANSWER.—In chronic myelogenous leukemia of this type, pregnancy may be allowed to proceed to its normal termination with the expectancy of a perfectly normal child. If roentgen treatment is given during pregnancy the child may be adversely affected, although there is a possibility that it may escape injury. In this case the fetus was between 4 and 6 weeks old when 120 roentgens were given, presumably over a remote region. It is probable that no damage was done, although it is impossible to predict absolutely. Roentgen therapy should be avoided and should not be given just because the leukocyte count is moderately high (25,000 to 50,000). Pregnancy alone, apparently, does not affect the course of the chronic form of the disease adversely, but the disease may be aggravated by premature termination of the pregnancy. The main problem is hemorrhage during delivery. Bleeding in chronic myelogenous leukemia is due mainly to the inadequate clot formation as a result of the excess of leukocytes. This condition is not influenced by the ordinary hemostatics but responds only when the leukocyte count is reduced by roentgen therapy before delivery. If the count can be reduced by treatment over the chest or spleen, the desired result may be obtained but the child may be injured. The same danger of hemorrhage is present, however, when cesarean section is attempted. Prophylactically, transfusions of 500 cc. of human serum may be given intravenously just before delivery. If it is necessary to give intensive roentgen therapy during the course of the disease, the pregnancy must be terminated prematurely.

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POSSIBLE LATE MENOPAUSAL SYMPTOMS

To the Editor:—A woman in her sixties, long past the menopause, says that she has had "hot flashes" several times a day for the last thirty years. These attacks are becoming more frequent and are preceded by a period of profound depression. The latter is more distressing to the patient than the hot flashes. There are no positive physical findings. Is there anything beside estrogenic hormones, which I am trying, that would make the vasomotor system any more stable?

George C. Christie, M.D., Canon City, Colo.

ANSWER.—While the duration of the vasomotor symptoms of the menopause, like their severity, is variable, such symptoms are rarely troublesome beyond a period of a few years, but in diminishing form they may continue longer. The term "hot flashes" refers to the hot, tingling sensations which often involve the whole body. The much more frequent "hot flushes" involve chiefly the head, neck and upper thorax, and it is possible that it is these of which the patient complains. There is general agreement that the entire group of vasomotor symptoms, including the characteristic sweats with the two already mentioned, is brought about by withdrawal of the estrogenic ovarian secretion, with consequent disruption of the reciprocal relations between ovarian and pituitary function. Aside from other evidence, symptoms of a second menopause have been noted in old women after the removal of the estrogen-producing granulosa-cell types of ovarian tumor (Novak, Schulze, Dworzak).

Moreover, it is now known that estrogen is produced in the bodies of at least a proportion of postmenopausal or even castrated women. The exact source of this production is not known, but the evidence points to one of the other endocrine glands, probably the adrenal cortex. In any event, such estrogen production in women well beyond the menopause might be expected to bring about phases of ovarian-pituitary dysharmony not unlike that characterizing the menopause.

In the management of such cases, it is of prime importance to eliminate other possible causative factors. Chief among these is the neuropsychogenic element which so often confuses the picture of the normal menopause. It must be remembered too that somewhat similar vasomotor symptoms may occur in hyperthyroidism and in cases of so-called vasomotor instability. If practicable, studies of the vaginal smear and of the estrogenic and gonadotropic content of the urine may throw light on the problem in this case. The fact that the patient in question has apparently not responded to estrogenic treatment would suggest that they may not be of endocrine origin. On the other hand, perhaps the dosage has been insufficient. Menopausal symptoms of moderate severity would ordinarily be alleviated by doses of 10,000 international units given intramuscularly two or three times a week for from one or two to three or four injections. While other plans of treatment, such as irradiation of the ovary and hypophysis, have been suggested, they are, in the opinion of most gynecologists, associated with some hazard and are often ineffectual. For discussions of the general subject of menopausal therapy, including a consideration of dosage and routes of administration of estrogen, the possible hazards of overtreatment and the use of such nonhormonal estrogens as diethylstilbestrol, the correspondent may be referred to the following among many publications:

Novak, Emil: Management of the Menopause, *Am. J. Obst. & Gynec.* **40:** 589 (Oct.) 1940.
Shorr, Ephraim: The Menopause, *Bull. New York Acad. Med.* **16:** 453 (July) 1940.

RED BLOTCHES OF SKIN IN CONGESTIVE HEART FAILURE

To the Editor:—Recently I have had several patients with congestive heart failure who in the last few weeks had small red blotches over the body. They began as small areas and rapidly increased in number and size. The patients died soon after. The condition might be called morbus maculosus. Could you tell me what the underlying cause is, increased venous blood pressure, increased permeability of the capillaries or changes in the carbon dioxide and oxygen in the blood?

Elmer E. Kottke, M.D., Des Moines, Iowa.

ANSWER.—It is uncommon for congestive heart failure to be attended during the last few days or weeks of life with macular skin lesions such as those described. No one consulted has been willing to attribute such lesions to congestive heart failure per se. Purpura can sometimes be terminal, that is, in the last few hours of life, especially in the presence of abnormalities of the blood or of the blood vessels when increased permeability of the capillaries may be largely blamed. Of course, in conditions such as subacute bacterial endocarditis or active rheumatism, cutaneous lesions are not uncommon, but they are not merely terminal and they are not primarily due to congestive heart failure. Hence the presence of red blotches over the body in the presence of congestive heart failure demands a search for some cause other than the heart disease and failure themselves.

HEMORRHAGE, SHOCK AND NIKETHAMIDE DOSAGE

To the Editor:—Can you tell me whether there is danger from an overdose of nikethamide in the agonized patient? A woman apparently in agony received caffeine and nikethamide subcutaneously one hour after the transfusion of 300 cc. of blood and 1,000 cc. of 5 per cent dextrose solution. Later I gave her nikethamide slowly intravenously. As long as the drug was being administered, the pulse and the respiration remained fairly good, although consciousness was not regained. After 6 ampules had been given I stopped the administration of nikethamide because (1) it apparently prolonged agony without returning the patient to consciousness and (2) I was afraid of an eventual overdose. Soon the patient died. There was a bleeding ulcer of the duodenum, confirmed by autopsy. Can you tell me whether agony in itself, loss of consciousness, exophthalmos, deep, suffocated breathing and small quick pulse is a reversible condition, and how long it is reversible? Does it represent irreparable damage of the cortex of the brain or not? The postmortem examination of the patient, which showed the bowels full of blood, raises the third question: As all life-saving measures tend in themselves to raise blood pressure and increase bleeding, do you think it advisable to operate on such a patient? When the patient entered the hospital the hemoglobin content was 50 per cent.

M.D., Oregon.

ANSWER.—There is little danger of overdosage of nikethamide as the toxicity is low and the substance is rapidly detoxified in the body. Overdosage is conditioned not only on the size of the dose but on the rapidity with which the drug is given. The drug carries its own warning signal, as it becomes a convulsant before the lethal dose is approached.

The patient probably had a peripheral vascular collapse. When this occurs there is a deficient return flow to the heart. This deficient return flow comes about (1) when blood escapes from the vessels, (2) when plasma escapes into the tissues and (3) when the arteriolar bed dilates or blood collects in the viscera. In this case there was probably a combination of escape of blood from the hemorrhage from the ulcer and collection of blood in the viscera from a dilatation of the arteriolar bed. The result would be a tremendous fall in blood pressure and a diminished cardiac output. The hypotension and deficient cardiac output are accompanied by a deficient cerebral and coronary blood flow. If the blood flow in the cerebral and coronary circulation is deficient over a long enough time irreparable damage ensues and the condition is irreversible. If the collapse is overcome either by restoration of the vasomotor tone or by control of the hemorrhage, before irreparable damage ensues, the patient recovers. In cases of severe collapse it is often impossible to tell from the clinical symptoms whether the condition is reversible. In this case it seems fair to assume that the vasomotor tone was partially restored but the blood loss continued.

The question of operation requires the exhibition of most critical judgment. As a general proposition, the presence of shock or peripheral collapse is a contraindication to operation. Surgical shock added to peripheral collapse is likely to be fatal. It is conceivable that if bleeding were known to be going on and its source were known an attempt to stop the hemorrhage might be made. It seems more than likely that in the situation described the patient would have succumbed in any event.

SPASMODIC TORTICOLLIS

To the Editor:—Can you give me the consensus as to the operative results of section of the eleventh cranial nerve for so-called functional spasmodic torticollis? My patient has had severe spasms for the past four or five months. He has been examined by two neurologists, who agree that it comes under the heading of "functional spasmodic torticollis." Does simple crushing of the nerve as is performed in a temporary phrenic nerve paralysis offer any value?

M.D., New York.

ANSWER.—Since the cause of any one particular instance of spasmodic torticollis is seldom determined, adequate treatment may be lacking, and, in fact, any treatment of this condition may be and frequently is of little effect. That it may actually be on an organic basis and follow encephalitis, striatal disease or myositis seems entirely tenable. However, in most instances the condition is believed to be on a functional basis, and by far the larger number of such patients are helped by intelligent psychotherapy. Since in the usual case of torticollis many more muscles than the sternocleidomastoid are involved, it is not sufficient to cut the accessory nerve alone to arrest the spasms. This procedure has, by and large, been marked with failure, and crushing the nerve would not be recommended as either rational or useful. Some surgeons have, with moderate success, cut the posterior roots of the upper cervical cord, together with the accessory nerve on the involved side. Others have gone so far as to cut the anterior and posterior roots of the cervical cord, together with the accessory nerve on both sides, thereby destroying all efferent and afferent pathways of the cervical musculature. Then, of course, the neck could not be moved even by a hysterical person, but such radical surgery would seem to be

rarely if ever recommended. Operative results for spasmodic torticollis are poor; psychotherapy is the best means of treatment of the usual patient with this complaint; many cases will not respond to treatment of any kind.

SUBLUXATION OF RIB FROM LIFTING AND ABDOMINAL PAIN

To the Editor:—**While lifting a 90 pound roll of wire, a white man aged 35 suddenly experienced a severe pain in the back just to the right of the spine, over the twelfth rib. The past medical history is negative; there had been no previous back injury, and the patient is accustomed to handling objects weighing as much as 200 pounds. The pain was immediately relieved with diathermy but returned one hour later and required opiates. Twenty-four hours later he had sudden severe epigastric pain with generalized boardlike rigidity of the abdomen. Roentgenograms of the chest and abdomen were negative; roentgenograms of the thoracic spine revealed a slight separation of the twelfth right rib from the spinal attachment; the white blood count was 13,000 with 90 per cent polymorphonuclears; the temperature was 100.8 F.; urinalysis was negative; the blood Wassermann and Kahn reactions were negative, and the pulse was 72, full and regular. In view of the history of injury it was decided to treat the patient conservatively, and the following day his condition remained unchanged with the exception of occasional emesis of undigested food and bile; his morning white blood count was 20,000, dropping to 10,000 by evening. Infusion of 5 per cent dextrose solution was followed by a chill and a temperature of 104 F. Three hours later his temperature dropped to 100 F., and the pain and rigidity disappeared from the abdomen. The following morning the patient was comfortable except for pain in the back, and he has continued to improve daily. Surgical consultation was called with the development of the epigastric pain, and the surgeon felt that there was probably a coincidental perforated ulcer which had sealed off. I should like to know whether the rapid improvement of abdominal symptoms is compatible with such a diagnosis and whether this severe epigastric pain could be due to an injured intercostal nerve or a diaphragmatic injury even though the roentgenograms of the diaphragmatic area were negative.**

M.D., Iowa.

ANSWER.—After consideration of the evidence given in this case, there is no hesitation in stating that such a train of symptoms as detailed in the report could not come from a subluxation of so small a joint as the twelfth rib. The patient might have a little local tenderness which would last a varying length of time, but the other symptoms would not be present. This man probably had one of three conditions in the abdomen: 1. A perforating ulcer is possible which sealed itself over. In a flat chested man with the liver pressed closely down over the duodenum, one of these perforations can be shut off and walled in with great rapidity. 2. If the patient had a barrel shaped chest, one would have to seek another explanation. In this type of individual one would suspect an acute cholecystitis with an obstruction of the cystic duct of a ball valve type which relaxed and permitted a free flow of bile, thus relieving the symptoms. 3. The third possibility would be an acute appendicitis of an obstructive type in which the obstruction is relieved and the inflammatory mass empties into the bowel. Either of the conditions detailed in 2 and 3 could give the symptom complex as shown in the report. The speed of repair and convalescence following 2 and 3 would be far more rapid than in 1.

THERAPY OF HYPOPARATHYROIDISM

To the Editor:—**A woman who had a thyroidectomy about five years ago, has received oral calcium and parathyroid since the operation. Without the calcium she quickly develops signs of hypothyroidism with tetany. For the past two months the parathyroid has not seemed to work, and it has been necessary to give calcium intravenously in order to maintain the blood calcium anywhere near normal. Calcium gluconate intravenously in her case does not give as complete relief from symptoms as calcium chloride intravenously, which is being used at present. This, of course, reduces the heart rate to less than 50 at the time of administration. The patient also has hypertension and chronic gallbladder disease. I should like to know as to the advisability of continuing the use of the intravenous calcium chloride over a long period of time, whether or not it is contraindicated, and any suggestion as to therapy if it becomes necessary to discontinue this form of therapy.**

J. F. Rommel, M.D., Oneida, N. Y.

ANSWER.—The therapy of hypoparathyroidism is now simple and satisfactory. The intravenous administration of calcium salts is no longer necessary except in an acute emergency. Then calcium gluconate is preferable to calcium chloride, since it is less irritating. Dihydrotachysterol is capable, when administered by mouth, of raising the serum calcium value to normal and thus of overcoming most of the symptoms of hypoparathyroidism. One usually starts with 5 mg. of this substance daily for about five days and later reduces the dosage to 5 mg. three times a week. The only danger to keep in mind is the possibility of producing hypercalcemia. This danger has been overemphasized in the past, however. It may be guarded against by doing rough tests for calcium in the urine with the use of the Sulkowitch reagent. Further details are given by Fuller Albright (Note on the Management of Hypoparathyroidism with Dihydrotachysterol, THE JOURNAL, June 24, 1939, p. 2592).

PROBABLE SCLEROSING OSTEITIS OF GARRÈ

To the Editor:—**A man in his thirties who was operated on one year ago for acute osteomyelitis of the femur has suffered from furunculosis for years. He states that Staphylococcus albus was isolated. At present he has a discharging sinus on the upper outer side of the thigh which necessitates the wearing and changing of daily dressings. At present the roentgenograms show fusiform thickening of the cortex of the upper third of the left femur just below the lesser and greater trochanters, more evident at the site of the lesser trochanter. This fusiform swelling is due to some irregular bone formation derived from the outer portion of the cortex and the periosteum. No evidence of sequestrum or cavities is seen. The findings indicate a chronic osteomyelitis of long standing. I have curetted the walls of the sinus and removed a valvelike membrane which obstructed the opening. The sinus is 1½ inches long. I packed it with sterile sulfanilamide daily for a week. At present I am packing the sinus with a drain saturated with azochloramid in olive oil 1: 2,000 every four days. The discharge at present is seromucous. I should like to know how this sinus can be healed.**

M.D., New Bedford, Mass.

ANSWER.—From the description of the roentgenograms it would seem that this condition might be due to an osteitis known as the sclerosing, nonsuppurative type originally described by Garrè. However, the name is misleading, for sometimes osteitis of this kind does break down and suppurate and drainage occurs, but usually there is no sequestrum. If there is a sequestrum, it is small. If there is no sequestrum and no central bone abscess in this case (which should be apparent in the roentgenogram if present), it might be well to try swabbing out the sinus every day with a solution of equal parts of phenol (carbolic acid) and tincture of iodine, being careful to protect the skin edges with an alcohol pad while this is being done. Sometimes this solution will destroy the granulating tissues and scarify the sinus tract, causing the walls to collapse, adhere and thus close the tract. If treating the condition in this manner every day for ten days or two weeks does not result in improvement, the treatment should be discontinued. One might also try injecting the sinus tract with a solution of sulfathiazole and sesame oil. Sufficient sulfathiazole should be put in the sesame oil to produce a thick, pasty solution which can be injected into the sinus. This should be repeated daily for several weeks.

There is no royal road to the healing of sinuses due to osteomyelitis. The main point is to be certain that there is no dead bone present, for, if there is, treatment will not produce results. Sequestrums must be removed or work their own way out.

PAINFUL PAROXYSMS OF JAW

To the Editor:—**A housewife aged 45, who has been known to have diabetes for the past eight years, has been taking insulin for only three months, 50 units daily, and has the diabetes well controlled. About two months ago she had a set of dentures made and complained of no trouble until three weeks ago. Then suddenly she experienced excruciating pain in the lower jaw on taking the first bite at mealtime. The pain is bilateral and around the angle of the jaw; it does not radiate and is described as a severe shooting sensation. She has to grab her jaw with both hands until the sensation subsides. After the momentary pain subsides she can eat the remainder of the meal in comfort. Oddly enough, fluids also produce the pain, which is not related, apparently, to motion at the articulation; thus she gets the pain on taking orange or tomato juice, but milk, tea and coffee produce no ill effects. I sent her to a dentist to ascertain what role the new dentures might be playing as a cause of such pain. He thought that pressure on the long buccal nerve might be the cause, and on infiltration with procaine hydrochloride the patient had complete though temporary relief. Accordingly the dentures were filed down to alter the bite somewhat, but the patient continues to look forward to each meal with dread because the pain continues unabated. I find this case so unusual that I write to ask your opinion and suggestions.**

M.D., New York.

ANSWER.—The data presented are not sufficient to permit a diagnosis in this case. The painful paroxysms are not typical of trifacial neuralgia, and the diabetes probably has no direct etiologic bearing. While a change in the dental bite resulting from the dentures may have produced some alteration in the temporomaxillary articulations, it is not likely that this has any direct bearing.

The character and distribution of the pain suggest a muscle spasm or a transitory obstruction of the parotid ducts. The latter is supported by the fact that fruit juices, which tend to stimulate profuse secretion of saliva, induce the pain, whereas bland fluids do not. It is possible that trauma or irritation to the meatuses of Stensen's ducts attributable to the dentures may have a direct causative effect.

In all probability the painful paroxysms will disappear spontaneously in the course of time, and leaving the dentures out for a while is likely to hasten this.

LOCALIZED YELLOW DISCOLORATION OF SKIN AND AMENORRHEA IN YOUNG WOMAN

To the Editor:—A young woman aged 17, well nourished and healthy looking, ceased to menstruate three years ago. All laboratory analyses were made and nothing abnormal was found; the blood chemistry was somewhat increased. Examination of the heart, lungs, pelvis and so on revealed no abnormalities. Psychically she seems somewhat deviated from the normal; there are spells of melancholy and excited states. She has had much estrogenic therapy by mouth and enterically with heavy dosage but so far to no effect. Her mind is much disturbed by the fact of menstruation not appearing. She has a peculiar icteric discoloration of the skin of the hands and feet only. The skin of the rest of the body is clear, as is the sclera of both eyes. There are no clay colored stools. Can you help me as to the cause of the color of the skin of her hands and feet and the probable cause of her lack of menstruation? The estrogenic products were of different reliable manufacture.

M.D., Iowa.

ANSWER.—It is presumed that the usual liver function tests have been performed and have failed to reveal liver damage. There is a possibility that the peculiar discoloration in this case is due to carotenemia rather than to a derangement in the liver or gallbladder. In cases of carotenemia there is rarely any discoloration of the conjunctiva but the change is localized elsewhere. Some obese women who are on a rigid diet eat an excessive amount of carrots and develop carotenemia. If this is true in this case, carrots should be omitted from the diet. Even if the patient is not consuming large amounts of carrots, it may be advisable to omit them for a while.

It is unfortunate that the tests failed to reveal any specific abnormality, because most likely in this case the persistent amenorrhea is due to some general disturbance. Estrogen therapy may produce bleeding but it will not be periodic unless the treatment is carried out repeatedly. This, of course, is not true menstruation. More logical therapy for the amenorrhea is the use of pituitary preparations or gonadotropic hormone from mare's serum, but both of these preparations yield successful results in only a small proportion of amenorrheic women.

YEAST INFECTION OF VAGINA IN PREGNANCY

To the Editor:—A patient pregnant about six months showed on antepartum examination a yeast infection of the vagina. There are always thick chunks of cheesy material present which, on microscopic examination, show the yeast organisms. I have treated the patient with compound solution of iodine and methylrosaniline with no result. Could this yeast infection produce a serious infection during the puerperium? How long do you think I should continue local treatment in this case? As a rule, I do not touch the vagina, if possible, during the last weeks of pregnancy. This patient otherwise is healthy. There is no sugar in the urine. Could you advise me what to do to get rid of this infection?

Ludwig Gruenewald, M.D., Sheboygan, Wis.

ANSWER.—Yeast infections of the vulva and vagina are more common in pregnant women than in the nonpregnant. In some pregnant women the condition persists despite treatment but disappears spontaneously soon after delivery. It may, however, reappear later. There need be little fear about puerperal infection arising from the yeast infection. Nevertheless the condition should be treated even during the last few weeks of pregnancy to give the patient relief from itching and other symptoms. In nearly all cases, temporary benefit can be obtained by thorough application of 1 to 2 per cent solution of methylrosaniline to all parts of the vulva and vagina. This treatment should be carried out every second day for four or five times or until the discharge and its symptoms disappear. In some cases element iodine as found in 0.5 to 0.25 strength compound solution of iodine or 0.25 to 0.20 strength tincture of iodine is helpful.

SLOUGHING FROM SCLEROSING SOLUTIONS

To the Editor:—On two occasions after the injection of sodium morrhuate into a vein on the leg of a young unmarried woman there was a leakage into the surrounding tissues. Is this due to any peculiar porosity of the vein or is this drug more likely to filter through than some of the other drugs employed? Can you refer me to any literature bearing on these points?

M.D., Massachusetts.

ANSWER.—Perivenous infiltration or necrosis occurs following the injection of sclerosing solutions when the tip of the needle slips out of the vein or when the wall of the vein is infiltrated with the solution. Occasionally, however, a small area of sloughing may occur at a considerable distance from the site of injection, at a point where the wall of the vein is thin and closely adherent to the skin. In the presence of small, thin walled intracutaneous varicosities it is safer to use a 50 per cent dextrose or a 10 per cent sodium chlorite solution, because more active solutions may produce a necrosis of the wall. Further safeguards against sloughs following the injection treatment are the employment of fine, 23 to 25 gage, needles with short bevels, a free flow of blood on aspiration and a continuous watch for edema or blanching around the vein during the injection. If the perivenous injection is promptly stopped and the area around the vein is infiltrated with procaine hydrochloride, physiologic solution of sodium chloride, or the patient's own blood, a cutaneous necrosis may often be averted.

A pamphlet of the American Medical Association on varicose veins, reprinted in 1940, gives more detailed information on the subject. It can be obtained on application.

MEDICINAL USES OF FLAXSEED

To the Editor:—Does flaxseed tea, used over a period of weeks or months, in amounts of 2 cups a day, have any irritating gastric effect, such as nausea or injurious action on the bowel? Does it leave an acid residue? I have been unable to find the answer to these questions in any books available to me. Can you advise where I might get a satisfactory treatise on flaxseed and its medicinal actions?

L. C. Mudd, M.D., San Francisco.

ANSWER.—Flaxseed, a synonym for linseed, is said to have the properties of a demulcent and emollient because of the mucilage and oil it contains. Although an infusion has in the past enjoyed varying popularity in the therapeutics of the respiratory and urinary tracts, present evidence indicates that any therapeutic value of linseed probably is confined to its use as an emollient poultice and as a demulcent. The daily use of dilute solutions of flaxseed "tea" should not cause any gastrointestinal irritation. It does not leave an acid residue. Sources of information on the Linum, U. S. P., and Linaceae (flax family) are:

Second Supplement to the Pharmacopeia of the United States of America (U. S. P. XI, 1939 Supplement).
Mansfield, W. W.: Materia Medica, Toxicology and Pharmacognosy, St. Louis, C. V. Mosby Co., 1937.
Youngken, H. W.: A Textbook of Pharmacognosy, Philadelphia, P. Blakiston's Son & Co., 1936.
The Dispensatory of the United States of America, Philadelphia, J. B. Lippincott Company, 1937.

The last named publication contains the following pertinent statement on the use of flaxseed: "There is a popular notion that the mucilaginous substances can be absorbed from the alimentary tract and exercise an internal demulcent action, and an infusion made by treating the whole seeds with boiling water is widely employed in cartarrhs of the respiratory or urinary tracts. But as the gums, like other carbohydrates, are affected by digestive juices, no benefit is to be expected from such a use of the drug."

REPAIR OF THORACOTOMY WOUNDS

To the Editor:—Would you be kind enough to refer me to any articles on the plastic surgical repair of old deforming thoracotomy wounds?

Joseph L. Gaster, M.D., Brooklyn.

ANSWER.—A satisfactory article dealing with this subject has not been found. Plastic repair of deforming, completely healed thoracic wounds is rarely undertaken, partly because they may be covered by clothing and partly because the depression produced by the loss of ribs cannot adequately be overcome. Ugly, broad, depressed scars resulting from the healing of infected wounds may be excised, the extracostal muscle layer freed from binding scar tissue, and the muscles and skin sutured in separate layers. Primary union and a considerable improvement in the appearance of the wound may be expected if the suturing has been accomplished without tension.

Deforming, unhealed thoracic wounds, in the depth of which the lung and bronchial fistulas are exposed, present a complicated problem. When the lung is not the site of residual infection and when there is little or no wound discharge or sputum, the defect may be closed by pedicled grafts of muscle or skin. When infected, such closure cannot be effected until the pulmonary infection has been overcome either by the adequate drainage of residual abscesses, by the removal of bronchiectases by lobectomy or by other means.

VITAMINS AND DEAFNESS

To the Editor: — In the Oct. 25, 1941, issue of The Journal, page 1491, there is an answer to a question headed "Vitamins and Deafness." The answer contains a quotation at some length of comments made by Dr. George E. Shambaugh Jr. but leaves out an interesting discussion by H. E. Harris and P. R. Moore of the Crile Clinic, which appeared in the *Medical Clinics of North America* 24:533 (March) 1940. This discussion gives a quite different view of the subject than do the comments quoted from Shambaugh. I should like to point out also that I have never claimed that vitamins would completely restore loss of hearing caused by deafness due to eighth nerve involvement.

Grant Selfridge, M.D., San Francisco.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, JULY-DECEMBER, 1941

Titles have been listed or Abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past six months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1932. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

Acta chirurgica Scandinavica. Stockholm.
Acta medica Scandinavica. Stockholm.
Acta obstetricia et gynecologica Scandinavica. Stockholm.
Acta medica URSS. Moscow.
Acta orthopaedica Scandinavica. Copenhagen.
American Heart Journal. St. Louis.
American Journal of Cancer. New York.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Fort Wayne, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Cincinnati.
American Journal of Orthopsychiatry. Menasha, Wis.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Physiology. Baltimore.
American Journal of Psychiatry. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Review of Tuberculosis. New York.
Anais brasileiros de ginecologia. Rio de Janeiro.
Anales de la Cátedra de patología y clínica de la tuberculosis. Buenos Aires.
Anales de la Facultad de medicina de Montevideo.
Anales de la Sociedad de puericultura de Buenos Aires.
Anesthesiology. New York.
Annales pædiatrici. Basel.
Annali d'igiene. Rome.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of the Rheumatic Diseases. London.
Annals of Surgery. Philadelphia.
Archiv für Dermatologie und Syphilis. Berlin.
Archiv für Gynäkologie. Berlin.
Archiv für japanische Chirurgie. Kyoto.
Archiv für Kinderheilkunde. Stuttgart.
Archiv für klinische Chirurgie. Berlin.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Disease in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M. A., Chicago.
Archives of Physical Therapy. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivos argentinos de pediatría. Buenos Aires.
Archivos argentinos de tisiología. Buenos Aires.
Archivos de la Clínica e Instituto de endocrinología. Montevideo.
Archivos latino americanos de cardiología y hematología, Paseo de la Reforma. México, D. F.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Arkhiv Biologicheskikh Nauk. Leningrad.
Bahia medica. Bahia, Brazil.
Beiträge zur Klinik der Tuberkulose. Berlin.
Beiträge zur klinischen Chirurgie. Berlin.
Bibliotek for læger. Copenhagen.
Boletín del Instituto de medicina experimental para el estudio y tratamiento del cáncer. Buenos Aires.
Boletín de la Oficina sanitaria panamericana. Washington, D. C.
Boletín de la Sociedad cubana de pediatría. Havana.
Bollettino. Milan.
Boletines y trabajos, Academia argentina de cirugía. Buenos Aires.
Brain. London.
British Heart Journal. London.
British Journal of Children's Diseases. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Tuberculosis. London.
British Journal of Urology. London.
British Medical Journal. London.
Bulletin of the Health Organization of the League of Nations. Geneva.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the Naval Medical Association. Tokyo.
Bulletin of the New York Academy of Medicine. New York.
California and Western Medicine. San Francisco.
Canadian Medical Association Journal. Montreal.
Canadian Public Health Journal. Toronto.
Cancer Research. Baltimore.
Cardiologia. Basel.
Chirurg. Berlin.
Clinica. Bologna.
Clinica ostetrica e ginecologica. Rome.
Connecticut State Medical Journal. Hartford.
Cuore e circolazione. Rome.
Delaware State Medical Journal. Wilmington.
Der deutsche Militärarzt. Berlin.
Dermatologica. Basel.
Deutsche medizinische Wochenschrift. Leipzig.
Deutsche Zeitschrift für Chirurgie. Berlin.
Deutsches Archiv für klinische Medizin. Berlin.
Edinburgh Medical Journal.
Endocrinology. Springfield, Ill.
Folia Pharmacologica japonica. Kyoto.
Fortschritte auf dem Gebiete der Röntgenstrahlen. Leipzig.
Gann. Tokyo.
Gazzetta degli ospedali e delle cliniche. Milan.
Geneeskundig tijdschrift voor Nederlandsch-Indië. Batavia.
Giornale di clinica medica. Parma.
Giornale italiano di dermatologia e sifilologia. Milan.
Glasgow Medical Journal.
Hospital. Rio de Janeiro.
Illinois Medical Journal. Chicago.
Indian Medical Gazette. Calcutta.
Irish Journal of Medical Science. Dublin.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Endocrinology. Springfield, Ill.
Journal of Clinical Investigation. New York.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal-Lancet. Minneapolis.
Journal of Laryngology and Otology. London.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Muskegon.
Journal of the Missouri State Medical Association. St. Louis.
Journal of the National Cancer Institute. Washington, D. C.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology and Psychiatry. London.
Journal of Neurophysiology. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynaecology of British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. Cambridge
Journal of the Royal Army Medical Corps. London.

*Cannot be lent.

Journal of the South Carolina Medical Association. Florence.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Urology. Baltimore.
Kekkaku. Tokyo.
Kentucky Medical Journal. Bowling Green.
Klinicheskaya meditsina. Moscow.
Klinische Wochenschrift. Berlin.
Lancet. London.
Laryngoscope. St. Louis.
Maandschrift voor kindergeneeskunde. Leyden.
Mededeelingen van den dienst der volksgezondheid in Nederlandsch-Indië. Batavia.
Medical Annals of the District of Columbia. Washington.
Medical Journal of Australia. Sydney.
Medicina. México, D. F.
Medicine. Baltimore.
Medizinische Klinik. Berlin.
Medizinische Welt. Berlin.
Military Surgeon. Washington, D. C.
Minerva medica. Turin.
Minnesota Medicine. St. Paul.
Mitteilungen aus der medizinischen Akademie zu Kioto. Kyoto.
Monatsschrift für Geburtshülfe und Gynäkologie. Basel.
Monatsschrift für Kinderheilkunde. Berlin.
Münchener medizinische Wochenschrift. Munich.
Nagasaki Igakkai Zassi. Nagasaki.
Nebraska State Medical Journal. Lincoln.
Nervenarzt. Berlin.
New England Journal of Medicine. Boston.
New Orleans Medical and Surgical Journal.
New York State Journal of Medicine. New York.
New Zealand Medical Journal. Wellington.
Nordisk medicin. Stockholm.
North Carolina Medical Journal. Winston-Salem.
Northwest Medicine. Seattle.
Note e riviste di psichiatria. Pesaro.
Ohio State Medical Journal. Columbus.
Okayama-Igakkai-Zasshi. Okayama.
Ophthalmologica. Basel.
Oto-rino-laringologia italiana. Bologna.
Pennsylvania Medical Journal. Harrisburg.
Physiological Reviews. Baltimore.
Policlinico (sezione medica e pratica). Rome.
Practitioner. London.
Prensa médica argentina. Buenos Aires.
Presse médicale. Paris.
Psychiatric Quarterly. Utica, N. Y.
Psychoanalytic Quarterly. Albany, N. Y.
Public Health Reports. Washington, D. C.
Quarterly Journal of Medicine. Oxford.
Quarterly Journal of Studies on Alcohol. New Haven, Conn.
Radiology. Syracuse, N. Y.
Review of Gastroenterology. New York.
Revista argentina de neurología y psiquiatría. Rosario de Santa Fe.
Revista de la Asociación médica argentina. Buenos Aires.
Revista de cirugía de Buenos Aires.
Revista clínica española. Madrid.
Revista de gastro-enterologia de São Paulo.
Revista de higiene. Bogotá.
Revista médica brasileira. Rio de Janeiro.
Revista médica de Chile. Santiago.
Revista médica del Hospital general México, D. F.
Revista médica latino-americana. Buenos Aires.
Revista médica de Rosario. Rosario de Santa Fe.
Revista mexicana de cirugía, ginecología y cáncer. México, D. F.
Revista neurológica de Buenos Aires.
Revista de tuberculosis del Uruguay. Montevideo.
Revue belge des sciences médicales. Louvain.
Rhode Island Medical Journal. Providence.
Rivista di patologia e clinica della tubercolosi. Bologna.
Rivista di patologia nervosa e mentale. Florence.
Rocky Mountain Medical Journal. Denver.
Schweizerische medizinische Wochenschrift. Basel.
Sei-I-Kai Medical Journal. Tokyo.
South African Medical Journal. Cape Town.
Southern Medical Journal. Birmingham, Ala.
Southern Surgeon. Atlanta, Ga.
Southwestern Medicine. El Paso, Texas.
Sovetskaya meditsina. Moscow.
Sperimentale. Florence.
Surgery. St. Louis.
Surgery, Gynecology and Obstetrics. Chicago.
Taiwan Igakkai Zassi. Taihoku, Formosa.
Texas State Journal of Medicine. Fort Worth.
Tokyo Igakkwai Zassi. Tokyo.
Tubercle. London.
Ugeskrift for læger. Copenhagen.
Vestnik khirurgii. Leningrad.
Vestnik oftalmologii. Moscow.
Virginia Medical Monthly. Richmond.
Vrachebnoe delo. Kharkov.
War Medicine. Chicago.
Western Journal of Surgery, Obstetrics and Gynecology. Portland, Ore.
West Virginia Medical Journal. Charleston.
Wiener klinische Wochenschrift. Vienna.
Wiener medizinische Wochenschrift. Vienna.
Wisconsin Medical Journal. Madison.
Yale Journal of Biology and Medicine. New Haven.
Zeitschrift für die gesamte Neurologie und Psychiatrie. Berlin.
Zeitschrift für Kinderheilkunde. Berlin.
Zeitschrift für klinische Medizin. Berlin.
Zeitschrift für Urologie. Leipzig.
Zeitschrift für urologische Chirurgie. Berlin.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "SS," Student Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Acad.—Academy
Am.—American
A.—Association
Coll.—College
Conf.—Conference
Cong.—Congress
Cont.—Convention
Dist.—District
Hosp.—Hospital
Internat.—International
M.—Medical
Med.—Medicine
Nat.—National
Pharm.—Pharmaceutical
Phys.—Physicians
Rev.—Revision
Ry.—Railway
Soc.—Society
Surg.—Surgery
Surgs.—Surgeons
S.—Surgical

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